AUTHOR SEARCH

=> file caplus
FILE 'CAPLUS' ENTERED AT 15:34:09 ON 06 JUL 2005
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FILE COVERS 1907 - 6 Jul 2005 VOL 143 ISS 2
FILE LAST UPDATED: 5 Jul 2005 (20050705/ED)

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=> file medline
FILE 'MEDLINE' ENTERED AT 15:34:16 ON 06 JUL 2005

FILE LAST UPDATED: 5 JUL 2005 (20050705/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> d que L92
L1       214728 SEA FILE=MEDLINE ABB=ON  PLU=ON  (?ISCHEM? OR ?NEURODEGEN? OR
                ?NEUROPROTECT? OR ?ISCHAEM?)
L20             QUE  ABB=ON  PLU=ON  SHIMADA/AU
L21             QUE  ABB=ON  PLU=ON  "SHIMADA NAME NOT TRANSLATED"/AU
L22             QUE  ABB=ON  PLU=ON  "SHIMATA JUICHI"/AU
L23             QUE  ABB=ON  PLU=ON  "JUNICHI SHIMADA"/AU
L24             QUE  ABB=ON  PLU=ON  SUZUKI/AU
L25             QUE  ABB=ON  PLU=ON  "SUZUKI NAME NOT TRANSLATED"/AU
L26             QUE  ABB=ON  PLU=ON  "FUMIO SUZUKI"/AU
L27             QUE  ABB=ON  PLU=ON  IKEDA KEN?/AU
L28             QUE  ABB=ON  PLU=ON  "KUROKAWA M"/AU
L29             QUE  ABB=ON  PLU=ON  "KUROKAWA M S"/AU
L30             QUE  ABB=ON  PLU=ON  "KUROKAWA MASAKI"/AU
L31             QUE  ABB=ON  PLU=ON  "KUROKAWA MASAKO"/AU
L32             QUE  ABB=ON  PLU=ON  (L28 OR L29 OR L30 OR L31)
L33             QUE  ABB=ON  PLU=ON  "SHIMADA J"/AU
L34             QUE  ABB=ON  PLU=ON  "SHIMADA JUICHI"/AU
L35             QUE  ABB=ON  PLU=ON  "SHIMADA JUN"/AU
L36             QUE  ABB=ON  PLU=ON  "SHIMADA JUN ICHI"/AU
L37             QUE  ABB=ON  PLU=ON  "SHIMADA JUNICH"/AU
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                L38 OR L39)
L41             QUE  ABB=ON  PLU=ON  L20 OR L21 OR L22 OR L23 OR L40
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L43             QUE  ABB=ON  PLU=ON  "SUZUKI F F"/AU
L44             QUE  ABB=ON  PLU=ON  "SUZUKI FUMIO"/AU
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L47             QUE  ABB=ON  PLU=ON  "KUWANA Y"/AU
L48             QUE  ABB=ON  PLU=ON  "KUWANA YOSHIHISA"/AU
L49             QUE  ABB=ON  PLU=ON  "KUWANA YOSHIHIKO"/AU
L50             QUE  ABB=ON  PLU=ON  (L47 OR L48 OR L49)
L52         1630 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L27 OR L32 OR L41 OR L46 OR
                L50)
L53           37 SEA FILE=MEDLINE ABB=ON  PLU=ON  L52 AND L1
L54 (      28842)SEA FILE=CAPLUS ABB=ON  PLU=ON  (ISCHEMIA/CT OR "BLOOD VESSEL,
                DISEASE (L) ISCHEMIA"/CT OR "ISCHEMIA CARDIOVASCULAR SYSTEM"/CT
                 OR "BRAIN (L) CEREBRAL CORTEX, ISCHEMIA"/CT OR "BRAIN (L)
                HIPPOCAMPUS, ISCHEMIA"/CT OR "BRAIN (L) HIPPOCAMPUS, SECTOR
                CA1, ISCHEMIA"/CT OR "BRAIN (L) HIPPOCAMPUS, SECTOR CA1,
                PYRAMIDAL CELL LAYER, ISCHEMIA"/CT OR "BRAIN (L) ISCHEMIA"/CT
                OR "BRAIN (L) ISCHEMIA, FOCAL"/CT OR "BRAIN (L) ISCHEMIA,
                TRANSIENT"/CT OR "BRAIN (L) PROSENCEPHALON, ISCHEMIA"/CT OR
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                (L) STRIATUM, ISCHEMIA"/CT OR "BRAIN, DISEASE (L) FOREBRAIN,
                ISCHEMIA"/CT OR "BRAIN, DISEASE (L) HIPPOCAMPUS, SECTOR CA1,
                ISCHEMIA"/CT OR "BRAIN, DISEASE (L) HIPPOCAMPUS, SECTOR CA1,
                PYRAMIDAL CELL LAYER, ISCHEMIA"/CT OR "BRAIN, DISEASE (L)
                ISCHEMIA"/CT OR "BRAIN, DISEASE (L) PROSENCEPHALON, ISCHEMIA"/C
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                T)
L55 (       2518)SEA FILE=CAPLUS ABB=ON  PLU=ON  ("NERVE (L) ISCHEMIA"/CT OR
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                CENTRAL, DISEASE, ISCHEMIA"/CT OR "NERVOUS SYSTEM (L) CENTRAL,
                ISCHEMIA"/CT)
L56 (       4342)SEA FILE=CAPLUS ABB=ON  PLU=ON  ("ANTI-ISCHEMIC AGENTS"/CT OR
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                "ANTI-ISCHEMIA AGENTS"/CT OR "ANTI-ISCHEMIC DRUGS"/CT OR
                "ANTIISCHEMIA AGENTS"/CT OR "ANTIISCHEMIC AGENTS"/CT OR
                ANTIISCHEMICS/CT)
L57 (     22834)SEA FILE=CAPLUS ABB=ON  PLU=ON  ("CYTOPROTECTIVE AGENTS"/CT OR
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L62 (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  "JUNICHI SHIMADA"/AU
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L76 (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  "SHIMADA JUNICH"/AU
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L87 (        41)SEA FILE=CAPLUS ABB=ON  PLU=ON  "KUWANA YOSHIHISA"/AU
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                L89)
L91          21 SEA FILE=CAPLUS ABB=ON  PLU=ON  L58 AND L90
L92          47 DUP REMOVE L91 L53 (11 DUPLICATES REMOVED)
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=> d ibib abs hitind L92 1-47

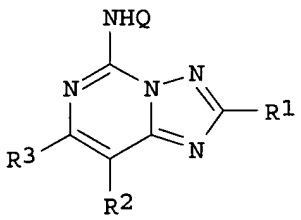
L92 ANSWER 1 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2004278861 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15178227
TITLE: T2-hypointensity in the cortex.
COMMENT: Comment on: J Neurol Sci. 2003 Jul 15;211(1-2):85-8. PubMed ID: 12767503
AUTHOR: Iwasaki Yasuo; Igarashi Osamu; Ichikawa Yasumitsu; Kiyozuka Tetsuhito; Kawabe Kiyokazu; Iguchi Hiroaki; Aoyagi Joe; Kawase Yuji; **Ikeda Ken**; Fujioka Toshiki
SOURCE: Journal of the neurological sciences, (2004 Jun 15) 221 (1-2) 121; author reply 123.
Journal code: 0375403. ISSN: 0022-510X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040606
Last Updated on STN: 20040820
Entered Medline: 20040819
CT Humans
Magnetic Resonance Imaging: MT, methods
Motor Neuron Disease: PA, pathology
*Motor Neuron Disease: PP, physiopathology
*Multiple System Atrophy: PA, pathology
***Neurodegenerative Diseases: PA, pathology**

L92 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:287848 CAPLUS
DOCUMENT NUMBER: 140:321375
TITLE: Preparation of 5-amino[1,2,4]triazolo[1,5-c]pyrimidine derivatives as antagonists of adenosine A2A receptor
INVENTOR(S): Iida, Kyoichiro; Sugita, Takamasa; Shiozaki, Shizuo; Kanda, Tomoyuki; **Kuwana, Yoshihisa**; **Shimada, Junichi**
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004029056	A1	20040408	WO 2003-JP12158	20030924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1544200 A1 20050622 EP 2003-753943 20030924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: JP 2002-276896 A 20020924
JP 2003-139994 A 20030519
WO 2003-JP12158 W 20030924
OTHER SOURCE(S): MARPAT 140:321375
GI



I

AB The title compds. [I; wherein R1 represents (un)substituted aryl or an (un)substituted aromatic heterocyclic group; R2 represents hydrogen, halogeno, lower alkyl, lower alkanoyl, aroyl, (un)substituted aryl, or an (un)substituted aromatic heterocyclic group; R3 represents lower alkyl, lower cycloalkyl, (un)substituted lower alkanoyl, (un)substituted aryl, an (un)substituted aromatic heterocyclic group, etc.; and Q represents hydrogen or 3,4-dimethoxybenzyl] or pharmacol. acceptable salts thereof are prepared These compds. have antagonistic activity on an adenosine A2A receptor and are useful for treatments for and/or prevention of diseases attributable to adenosine A2A receptor hyperenergia including Alzheimer's disease, progressive supranuclear paralysis, AIDS encephalopathy, transmissible spongiform encephalopathy (TSE), multiple sclerosis, amyotrophic lateral sclerosis, Huntington's disease, multiple system atrophy, cerebral hemorrhage, sleep disorder, ischemic heart diseases, and intermittent claudication. Thus, 600 mg 5-amino-2-(2-furyl)-7-(1,2,3,6-tetrahydropyridin-4-yl)-[1,2,4]triazolo[1,5-c]pyrimidine was dissolved in 10 mL DMF, treated with 0.300 mL 2-methoxy-1-bromoethane and 0.890 mL Et3N, stirred at room temperature for 11 h, concentrated under reduced pressure, and purified by silica gel chromatog. to give 90 mg 12 % 5-amino-2-(2-furyl)-7-[1-(2-methoxyethyl)-1,2,3,6-tetrahydropyridin-4-yl]-[1,2,4]triazolo[1,5-c]pyrimidine (II). II at 10-7 M inhibited the binding of [3H]CGS 21680 to adenosine A2A receptor of rat corpus striatum by 98%. Pharmaceutical formulations, e.g. an injection solution containing II, were described.

IC ICM C07D487-04
ICS A61K031-519; A61K031-5377; A61K031-55; A61K031-553; A61P009-00; A61P009-10; A61P021-00; A61P025-00; A61P025-14; A61P025-16; A61P025-20; A61P025-24; A61P025-28; A61P043-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Ischemia**
(cardiac; preparation of amino[1,2,4]triazolo[c]pyrimidine derivs. as antagonists of adenosine A2A receptor for prevention and/or treatment of diseases attributable to adenosine A2A receptor)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 3 OF 47 MEDLINE on STN

ACCESSION NUMBER: 2004576562 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15552868
TITLE: Argyrophilic grain disease clinically mimicking Parkinson's disease with dementia: report of an autopsy case.
AUTHOR: Uchikado Hirotake; Tsuchiya Kuniaki; Tominaga Itaru; Togo Takashi; Oshima Kenichi; Akiyama Haruhiko; **Ikeda Kenji**; Oda Tatsuro; Hirayasu Yoshio
CORPORATE SOURCE: Department of Psychiatry, Yokohama City University School of Medicine, Japan.
SOURCE: No to shinkei. Brain and nerve, (2004 Sep) 56 (9) 785-8. Journal code: 0413550. ISSN: 0006-8969.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CASE REPORTS) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041123
Last Updated on STN: 20041220
Entered Medline: 20041210

AB Argyrophilic grain disease (AGD) is a **neurodegenerative** dementia, which is neuropathologically characterized by the spindle-or comma-shaped argyrophilic grains scattered in the neuropil of hippocampal area. Several research reports have disclosed the pathological, biochemical and genetic characteristics of AGD, whereas the clinical aspects have not been fully investigated. Here we report an autopsy case of AGD. She developed tremor at age 63, and then developed dyskinesia, rigidity and gait disturbance. Thereafter, she had cognitive impairment and emotional disturbance at age 71, and died of pneumonia at age 76. She was clinically diagnosed as Parkinson's disease with dementia due to the presence of parkinsonism and dementia. Macroscopically, the brain demonstrated mild atrophy, and the weight was 1,240 g. Many argyrophilic grains were found in the hippocampus and amygdala. Coiled bodies and ballooned neurons were also present, while Alzheimer-type neurofibrillary changes were mild, consistent with stage 2 of Braak's classification. This case was neuropathologically diagnosed as AGD. In contrast, no remarkable pathological changes, including neuronal loss and Lewy bodies, were found in the nigra, locus ceruleus and basal nuclei. On the basis of the above-mentioned clinicopathological findings, parkinsonism with dementia is considered to be one of the clinical manifestations of AGD.

CT Check Tags: Female
Aged
*Brain: PA, pathology
*Dementia: PA, pathology
Diagnosis, Differential
English Abstract
Hippocampus: PA, pathology
Humans
Neurodegenerative Diseases: PA, pathology
*Parkinson Disease: PA, pathology
*Silver Staining
tau Proteins: ME, metabolism

CN 0 (tau Proteins)

L92 ANSWER 4 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2004143405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15037267
TITLE: Protective effects of **preischemic** treatment with pioglitazone, a peroxisome proliferator-activated

receptor-gamma ligand, on lung **ischemia**-reperfusion injury in rats.

AUTHOR: Ito Kazuhiro; **Shimada Junichi**; Kato Daishiro; Toda Shogo; Takagi Tomohisa; Naito Yuji; Yoshikawa Toshikazu; Kitamura Nobuo

CORPORATE SOURCE: Department of Cardiovascular and Thoracic Surgery, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan.. kazuitoh@koto.kpu-m.ac.jp

SOURCE: European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery, (2004 Apr) 25 (4) 530-6.
Journal code: 8804069. ISSN: 1010-7940.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200404

ENTRY DATE: Entered STN: 20040324
Last Updated on STN: 20040430
Entered Medline: 20040429

AB OBJECTIVES: Lung injury induced by **ischemia**-reperfusion is the main cause of early graft failure after lung transplantation, which may result from oxygen-free radicals, inflammatory cytokine production, and polymorphonuclear leukocyte accumulation into the interstitium, resulting in severe lung edema. Peroxisome proliferator-activated receptor-gamma (PPAR-gamma) belongs to the nuclear receptor superfamily and has an anti-inflammatory effect by preventing the activation of transcription factors such as nuclear factor-kappaB (NF-kappaB). NF-kappaB regulates the expression of many genes of early response products in the development of acute inflammation. We examined the effects of pioglitazone, a synthetic ligand of PPAR-gamma, against lung **ischemia**-reperfusion injury in rats. METHODS: The left lungs of male Wistar rats were rendered **ischemic** for 90 min and then reperfused for 2 h. Treated animals received pioglitazone (10 mg/kg) 2 h before induction of **ischemia**. Lung injury was quantified in terms of lung microvascular permeability (Evans blue dye extravasation), tissue lipid peroxidation (thiobarbituric acid reactive substances), and tissue polymorphonuclear leukocyte accumulation (myeloperoxidase activity). The tissue concentrations of tumor necrosis factor-alpha (TNF-alpha) and cytokine-induced neutrophil chemoattractant-1 (CINC-1) were also measured. Statistical analyses were performed by one-way analysis of variance, followed by Sheffe's multiple comparison test. RESULTS: The lung vascular permeability in pioglitazone-treated animals was reduced by 55% of the increase of Evans blue dye extravasation relative to control animals ($P=0.003$). The protective effects of pioglitazone treatment were correlated with the reduction by 79% of the increase of thiobarbituric acid reactive substances ($P=0.045$) and the reduction by 58% of myeloperoxidase activity increase ($P<0.001$). The production of TNF-alpha was reduced by 63% of the increase ($P<0.001$) and the reduction of CINC-1 was 45% ($P<0.001$). Pioglitazone did not affect the lung in the sham animals. CONCLUSIONS: Pioglitazone treatment before **ischemia** attenuated lung **ischemia**-reperfusion injury in rats. The mechanism of these protective effects involves inhibition of the production of proinflammatory cytokines, polymorphonuclear leukocyte accumulation, and tissue lipid peroxidation, resulting in reduced lung edema.

CT Check Tags: Male
Animals

Capillary Permeability: DE, drug effects
Cytokines: BI, biosynthesis
Ligands
Lipid Peroxidation: DE, drug effects
Lung: BS, blood supply
Microcirculation: DE, drug effects
Peroxidase: ME, metabolism
*Protective Agents: TU, therapeutic use
Rats
Rats, Wistar
*Receptors, Cytoplasmic and Nuclear: ME, metabolism
Reperfusion Injury: ME, metabolism
Reperfusion Injury: PP, physiopathology
*Reperfusion Injury: PC, prevention & control
Respiratory Distress Syndrome, Adult: ME, metabolism
Respiratory Distress Syndrome, Adult: PP, physiopathology
*Respiratory Distress Syndrome, Adult: PC, prevention & control
*Thiazolidinediones: TU, therapeutic use
*Transcription Factors: ME, metabolism
RN 111025-46-8 (pioglitazone)
CN 0 (Cytokines); 0 (Ligands); 0 (Protective Agents); 0 (Receptors, Cytoplasmic and Nuclear); 0 (Thiazolidinediones); 0 (Transcription Factors); EC 1.11.1.7 (Peroxidase)

L92 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:85533 CAPLUS
DOCUMENT NUMBER: 140:297324
TITLE: T-588 Protects Motor Neuron Death Following Axotomy
AUTHOR(S): Iwasaki, Yasuo; Ichikawa, Yasumitsu; Igarashi, Osamu; Konno, Shingo; Aoyagi, Joe; **Ikeda, Ken**; Marabuchi, Sigeki; Ono, Satoshi; Iguchi, Hiroaki; Kawabe, Kiyokazu; Fujioka, Toshiki
CORPORATE SOURCE: Department of Neurology, Toho University Omori Hospital, Omori Ota-ku, Tokyo, Japan
SOURCE: Neurochemical Research (2004), 29(2), 403-406
CODEN: NEREDZ; ISSN: 0364-3190
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB R(-)-1-(benzo [b] thiophen-5-yl)-2-[2-(N,N-diethylamino)ethoxy] ethanol hydrochloride (T-588) enhances acetylcholine release. This compound slows the motor deterioration of wobbler mouse motor neuron disease and enhances neurite outgrowth and choline acetyltransferase activity in cultured rat spinal motor neurons. We examined the ability of T-588 on axotomized spinal motor neuron death in the rat spinal cord. After the postnatal unilateral section of sciatic nerve, there was approx. a 50% survival of motor neurons in the fourth lumbar segment. In comparison with vehicle, i.p. injection of T-588 for 14 consecutive days rescued spinal motor neuron death. Our results showing in vivo neurotrophic activity of T-588 for motor neurons support the applicability of T-588 for the treatment of motor neuron diseases, such as amyotrophic lateral sclerosis and motor neuropathies.
CC 1-11 (Pharmacology)
IT **Cytoprotective agents**
(**neuroprotective**; T-588 protects motor neuron death following axotomy)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 6 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2004029513 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14730711
TITLE: Microglial tau undergoes phosphorylation-independent modification after **ischemia**.
AUTHOR: Uchihara Toshiki; Nakamura Ayako; Arai Tetsuaki; **Ikeda Kenji**; Tsuchiya Kuniaki
CORPORATE SOURCE: Department of Neuropathology, Tokyo Metropolitan Institute for Neuroscience, 2-6 Musashi-dai, Fuchu, Tokyo 183-8526, Japan.. uchihara@tmin.ac.jp
SOURCE: Glia, (2004 Jan 15) 45 (2) 180-7.
Journal code: 8806785. ISSN: 0894-1491.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040121
Last Updated on STN: 20040501
Entered Medline: 20040430

AB Tau2 is a phosphorylation-independent antibody that immunolabels neurofibrillary tangles (NFTs) of Alzheimer type and microglia around **ischemic** foci on formalin-fixed, paraffin-embedded sections. We found that copresence of polyethyleneglycol-p-isooctylphenyl ether (Triton X-100; TX) with tau2 abolished its immunoreactivity (IR) in these microglia but not its IR on NFTs. Tau2-immunoreactive bands, exclusively retrieved in Tris-soluble fraction of brain homogenates from **ischemic** foci, normal human and bovine brains, were of similar electrophoretic mobility, indicating that tau2 IR in these microglia is unrelated to hyperphosphorylation of tau. These tau2-immunoreactive bands except those from bovine brain were abolished in the copresence of TX. This was not due to washing out of tau, because similar immunoreactive bands were detectable with another antitau antibody even under a higher concentration of TX and because washing after TX exposure restored similar tau2 IR both on immunohistochemistry and immunoblot. These findings are explained if tau, modified after **ischemia**, undergoes a reversible conformational change on TX exposure. Because conformation at Ser101 of bovine tau is crucial for its affinity to tau2, this Ser-like conformation mimicked by its human counterpart Pro may represent pathological modification of tau shared by microglia around **ischemic** foci and NFTs. Relative resistance of tau2 epitope in NFTs to TX exposure suggests that tau woven into NFTs confers additional stability to this pathological modification on tau2 epitope. Susceptibility of tau2 epitope to TX, seen in these microglia, is shared with glial cytoplasmic inclusions and will show its conformational state to be different from that in NFTs.

CT Check Tags: Female; Male
Aged
Aged, 80 and over
Antibodies: IM, immunology
***Brain Ischemia: ME, metabolism**
Brain Ischemia: PA, pathology
Brain Ischemia: PP, physiopathology
*Cerebral Cortex: ME, metabolism
Cerebral Cortex: PA, pathology
Cerebral Cortex: PP, physiopathology
*Cerebral Infarction: ME, metabolism
Cerebral Infarction: PA, pathology

Cerebral Infarction: PP, physiopathology
Epitopes: IM, immunology
Humans
Immunohistochemistry
Inclusion Bodies: IM, immunology
*Microglia: ME, metabolism
Microglia: PA, pathology
Middle Aged
Molecular Conformation
Neurofibrillary Tangles: IM, immunology
Neurofibrillary Tangles: ME, metabolism
Octoxynol
Phosphorylation
*Protein Processing, Post-Translational: PH, physiology
Research Support, Non-U.S. Gov't
Serine: IM, immunology
Serine: ME, metabolism
*tau Proteins: ME, metabolism
RN 56-45-1 (Serine); 9002-93-1 (Octoxynol)
CN 0 (Antibodies); 0 (Epitopes); 0 (tau Proteins)

L92 ANSWER 7 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2004007026 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14705114
TITLE: Identification of amino-terminally cleaved tau fragments that distinguish progressive supranuclear palsy from corticobasal degeneration.
AUTHOR: Arai Tetsuaki; **Ikeda Kenji**; Akiyama Haruhiko; Nonaka Takashi; Hasegawa Masato; Ishiguro Koichi; Iritani Shuji; Tsuchiya Kuniaki; Iseki Eizo; Yagishita Saburo; Oda Tatsuro; Mochizuki Akihide
CORPORATE SOURCE: Department of Psychogeriatrics, Tokyo Institute of Psychiatry, Setagaya-ku, Tokyo, Japan.. aria@prit.go.jp
SOURCE: Annals of neurology, (2004 Jan) 55 (1) 72-9.
Journal code: 7707449. ISSN: 0364-5134.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040106
Last Updated on STN: 20040313
Entered Medline: 20040312

AB Progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) are **neurodegenerative** diseases that are characterized by intracytoplasmic aggregates of hyperphosphorylated tau with four microtubule-binding repeats. Although PSP and CBD have distinctive pathological features, no biochemical difference in aggregated tau has been identified. In this study, we examined the brains of eight patients with PSP, six patients with CBD, and one atypical case with pathological features of both CBD and PSP. On immunoblots of sarkosyl-insoluble brain extracts, a 33kDa band predominated in the low molecular weight tau fragments in PSP, whereas two closely related bands of approximately 37kDa predominated in CBD. Immunoblots of the atypical case showed both the 33kDa band and the 37kDa doublet. Protein sequencing and immunochemical analyses showed that the 33kDa band and the 37kDa doublet consisted of the carboxyl half of tau with different amino termini. These results suggest that, despite the identical composition of tau isoforms, different proteolytic processing of abnormal tau takes place in these two diseases.

Such a biochemical divergence may be related to the neuropathological features of these diseases.

CT Check Tags: Comparative Study; Female; Male
Aged
Aged, 80 and over
Amino Acid Sequence
Basal Ganglia: ME, metabolism
Basal Ganglia: PA, pathology
Brain: ME, metabolism
*Brain: PA, pathology
*Brain Chemistry
Cerebral Cortex: ME, metabolism
Cerebral Cortex: PA, pathology
Humans
Immunoblotting
Immunohistochemistry
Middle Aged
Molecular Sequence Data
*Supranuclear Palsy, Progressive: ME, metabolism
Tauopathies: ME, metabolism
*tau Proteins: CH, chemistry
tau Proteins: ME, metabolism

CN 0 (tau Proteins)

L92 ANSWER 8 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2003564189 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14586629
TITLE: Expression of BRI, the normal precursor of the amyloid protein of familial British dementia, in human brain.
AUTHOR: Akiyama Haruhiko; Kondo Hiromi; Arai Tetsuaki; **Ikeda Kenji**; Kato Masanori; Iseki Eizo; Schwab Claudia; McGeer Patrick L
CORPORATE SOURCE: Tokyo Institute of Psychiatry, 2-1-8 Kamikitazawa, Setagaya-ku, 156-8585, Tokyo, Japan.. akiyama@prit.go.jp
SOURCE: Acta neuropathologica, (2004 Jan) 107 (1) 53-8. Electronic Publication: 2003-10-29.
Journal code: 0412041. ISSN: 0001-6322.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20031216
Last Updated on STN: 20040505
Entered Medline: 20040503

AB Familial British dementia (FBD) is characterized neuropathologically by deposition of a unique amyloid-forming protein, ABri. It is a fragment of an abnormal form of a precursor protein, BRI. In FBD, BRI is elongated by 11 amino acids due to a point mutation that prevents recognition of the normal stop codon. We have investigated the expression of normal BRI in non-FBD cases. Three antibodies were raised against sequences of BRI and were used for immunoblotting and immunohistochemistry. Each of these antibodies detected a band at approximately 35 kDa by Western blotting. In postmortem human brain tissues, BRI was detected as fine granules in the neuronal cytoplasm. Pyramidal neurons in CA3 and CA4 of the hippocampus as well as Purkinje cells in the cerebellar cortex were most intensely stained for BRI. Such a distribution of neurons strongly expressing BRI parallels the reported occurrence of ABri deposits in patients with FBD. In pathological cases, BRI was detected in dystrophic

neurites in senile plaques, around lesions in **ischemic** cases, in torpedo and glumose changes in the cerebellum, Lewy neurites, ballooned neurons, and neurons generally in hypoxic cases. These results suggest that BRI is transported in neuronal processes and is possibly involved in some role in nerve terminals. While a physiological role of BRI in brain remains to be determined, the behavior of BRI in diverse brain lesions appears to be somewhat analogous to that of amyloid precursor protein, which is the source of the beta-amyloid protein of Alzheimer's disease.

CT Check Tags: Female; Male
Adult
Aged
Aged, 80 and over
*Amyloid: ME, metabolism
Case-Control Studies
*Cerebellar Cortex: PA, pathology
*Dementia: PA, pathology
*Hippocampus: PA, pathology
Humans
Immunoblotting
Immunohistochemistry
Middle Aged
*Neurons: PA, pathology
Peptide Fragments: ME, metabolism
Research Support, Non-U.S. Gov't

CN 0 (Amyloid); 0 (ITM2B protein, human); 0 (Peptide Fragments)

L92 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:974369 CAPLUS
DOCUMENT NUMBER: 141:102283
TITLE: PET imaging of adenosine A1 receptors with 11C-MPDX as an indicator of severe cerebral ischemic insult
AUTHOR(S): Nariai, Tadashi; Shimada, Yuhei; Ishiwata, Kiichi; Nagaoka, Tsukasa; **Shimada, Junichi**; Kuroiwa, Toshihiko; Ono, Ken-Ichiro; Ohno, Kikuo; Hirakawa, Kimiyoshi; Senda, Michio
CORPORATE SOURCE: Department of Neurosurgery, Tokyo Medical and Dental University, Tokyo, Japan
SOURCE: Journal of Nuclear Medicine (2003), 44(11), 1839-1844
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We examined whether measurement of the adenosine A1 receptor (A1-R) with PET can predict the severity of ischemic brain damage using an occlusion and reperfusion model of the cat middle cerebral artery (MCA) and [1-methyl-11C]8-dicyclopropylmethyl-1-methyl-3-propylxanthine (MPDX), a positron-emitting radioligand developed at our institution. Methods: Eighteen adult cats underwent PET measurement of cerebral blood flow (CBF), A1-R, central benzodiazepine receptor (BDZ-R), and glucose metabolism with 15O-labeled water, MPDX, 11C-flumazenil (FMZ), and 18F-FDG, resp. The right MCAs of 13 cats were transiently occluded via a transorbital approach with microvascular clips. CBF was measured before occlusion of MCA, during occlusion, and immediately after reperfusion. After CBF measurement, A1-R, BDZ-R, and 18F-FDG uptake were serially measured in the order listed. Two months later, the degree of ischemic damage was evaluated by T2-weighted MR images obtained with an animal MRI system and by anal. of histol. specimens. Five cats that received no operations were used as controls. Results: The cats that underwent occlusion were divided into 3 groups: cats that did not survive the first day because of severe

neurol. and systemic conditions (n = 4), cats that survived and had infarcted lesions in both the cortex and the striatum (n = 3), and cats that survived and had infarcted lesions only in the striatum (n = 6). CBF during occlusion of the MCA was significantly lower in all 3 ischemic groups than in the control group, but there was no significant difference among the ischemic groups. Right-to-left ratios of CBF and 18F-FDG uptake did not significantly differ among the groups. MPDX binding and FMZ binding were significantly lower in the groups with severe ischemic insult than in the groups with little to no insult. Conclusion: The degree of decreased MPDX binding to A1-Rs after reperfusion was a sensitive predictor of severe ischemic insult. MPDX PET has good potential to become a suitable in vivo imaging technique for evaluating the function of adenosine and A1-Rs in relation to cerebral ischemia.

CC 8-9 (Radiation Biochemistry)

IT Circulation
Ischemia
(cerebral; PET imaging of A1 receptors with 11C-MPDX as indicator of severe cerebral ischemic insult)

IT **Brain, disease**
(**ischemia**; PET imaging of A1 receptors with 11C-MPDX as indicator of severe cerebral ischemic insult)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2003:814585 CAPLUS
DOCUMENT NUMBER: 140:210465
TITLE: T-588 Protects Motor Neuron Death Against Glutamate-Induced Neurotoxicity
AUTHOR(S): Iwasaki, Yasuo; Ichikawa, Yasumitsu; Igarasi, Osamu; Aoyagi, Joe; Konno, Shingo; **Ikeda, Ken**; Iguchi, Hiroaki; Kawabe, Seiichi; Marubuchi, Shigeki; Ono, Satoshi
CORPORATE SOURCE: Department of Neurology, Toho University Omori Hospital, Tokyo, Japan
SOURCE: Neurochemical Research (2003), 28(12), 1829-1832
CODEN: NEREDZ; ISSN: 0364-3190
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To examine the possible neuroprotective effect of T-588 against glutamate-induced neurotoxicity, we analyzed the pharmacol. utility of T-588 in a postnatal organotypic culture model of motor neuron degeneration. Treatment with 10-5 M of glutamate resulted a motor neuron loss and decreased activity of choline acetyltransferase (ChAT). Cotreatment of 10-5 M of glutamate and T-588 revealed a protective effect against motor neuron death and decreased ChAT activity. We concluded that T-588 may play important roles in the survival and maintenance of spinal motor neurons in its neuroprotection against glutamate-induced neurotoxicity. Our data may provide a rationale for designing a therapeutic strategy for protection against pathol. induced motor neuron damage or cell death such as amyotrophic lateral sclerosis and motor neuropathy.

CC 1-11 (Pharmacology)

IT **Cytoprotective agents**
(**neuroprotective**; T-588 protects motor neuron death against glutamate-induced neurotoxicity)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 11 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2003160468 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12649507
TITLE: Increased expression of neuronal apolipoprotein E in human brain with cerebral infarction.
AUTHOR: Aoki Kazuko; Uchihara Toshiki; Sanjo Nobuo; Nakamura Ayako; **Ikeda Kenji**; Tsuchiya Kuniaki; Wakayama Yoshihiro
CORPORATE SOURCE: Department of Neuropathology, Tokyo Metropolitan Institute for Neuroscience, Fuchu, Japan.
SOURCE: Stroke; a journal of cerebral circulation, (2003 Apr) 34 (4) 875-80. Electronic Publication: 2003-03-20. Journal code: 0235266. ISSN: 1524-4628.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030406
Last Updated on STN: 20030425
Entered Medline: 20030424

AB BACKGROUND AND PURPOSE: Cellular origin of apolipoprotein E (ApoE) in the human brain and its roles in physiological and pathological conditions remain to be clarified. METHODS: Immunolocalization of ApoE was investigated in a series of autopsied human brains with or without infarction. ApoE expression was also estimated on immunoblot on protein extracts from autopsied brains and a cultured neuroblastoma cell line of human origin (GOTO) subjected to an oxidative stress induced by exposure to hydrogen peroxide (0.2 mmol/L). RESULTS: In addition to astrocytes and microglia, neurons and degenerated axons in and around the **ischemic** foci contained ApoE-like immunoreactivity, which was more intense in recent **ischemic** foci. Immunoblot demonstrated an increase in expression of ApoE in brain extracts from **ischemic** lesion, and this increase was also pronounced in the cultured neuroblastoma cell line after the stress. CONCLUSIONS: Accumulation of ApoE in neurons in and around **ischemic** foci of the human brain is related to an increase in ApoE synthesis in neurons, as seen in cultured neuronal cells after oxidative stress. Intrinsic regenerative activity of neuron in reaction to external insults may be related to this increase in ApoE of neuronal origin.

CT Check Tags: Female; Male
Aged
Apolipoproteins E: AN, analysis
*Apolipoproteins E: BI, biosynthesis
Apolipoproteins E: IM, immunology
Blotting, Western
Brain: CY, cytology
*Brain: ME, metabolism
*Cerebral Infarction: ME, metabolism
Humans
Immunohistochemistry
Middle Aged
*Neurons: ME, metabolism
Oxidative Stress
Research Support, Non-U.S. Gov't
Tumor Cells, Cultured
CN 0 (Apolipoproteins E)

L92 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2003:379985 CAPLUS
DOCUMENT NUMBER: 139:332928
TITLE: Temocapril prevents motor neuron damage and upregulation of cyclooxygenase-II in glutamate-induced neurotoxicity
AUTHOR(S): Iwasaki, Yasuo; Ichikawa, Yasumitsu; Igarashi, Osamu; **Ikeda, Ken**; Konno, Shingo; Aoyagi, Joe; Kinoshita, Masao
CORPORATE SOURCE: Fourth Department of Internal Medicine, Toho University Ohashi Hospital, Tokyo, Japan
SOURCE: Neurological Research (2003), 25(3), 301-304
CODEN: NRESDZ; ISSN: 0161-6412
PUBLISHER: Forefront Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To examine the possible neuroprotective effect of temocapril, one kind of angiotensin-converting enzyme inhibitor, against glutamate-induced neurotoxicity, we analyzed the pharmacol. utility of temocapril in a post-natal organotypic culture model of motor neuron degeneration. Treatment with 10-5 M of glutamate resulted in a motor neuron loss and decreased activity of choline acetyltransferase (ChAT). Cotreatment of 10-5 M of glutamate and temocapril revealed protective effect on motor neuron death and decreased activity of ChAT. Next we performed reverse transcription-PCR anal. for cyclooxygenase-II (COX-II). COD-II mRNA was upregulated in glutamate-treated culture. Cotreatment with temocapril and glutamate inhibited upregulation of COX-II. Taken together, temocapril may have therapeutic potential for diseases which associate with upregulation of COX-II, in addition to its role in glutamate excitotoxicity.

CC 1-11 (Pharmacology)
IT **Cytoprotective agents**
(**neuroprotective**; temocapril prevents motor neuron damage and upregulation of cyclooxygenase-II in glutamate-induced neurotoxicity)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:719963 CAPLUS
DOCUMENT NUMBER: 140:122511
TITLE: Protective effect of N-methyl-1-deoxynojirimycin on lung ischemia reperfusion injury: an in vivo study MdNM reduces lung ischemia reperfusion injury
AUTHOR(S): Ito, Kazuhiro; Shimada, Yasuyuki; Kato, Daishiro; **Shimada, Junichi**; Toda, Shogo; Kitamura, Nobuo
CORPORATE SOURCE: Dep. of Cardiovascular and Thoracic Surgery, Kyoto Prefectural University of Medicine, Kyoto, Japan
SOURCE: Junkan Seigyo (2003), 24(2), 135-137
CODEN: JUSEE7; ISSN: 0389-1844
PUBLISHER: Nippon Junkan Seigyo Igakkai
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The warm ischemic period following cardiac arrest damages the lungs. N-Methyl-1-deoxynojirimycin (MdNM) can preserve glycogen and reduce myocardial infarct size in rabbit heart. We tested the hypothesis that MdNM may reduce ischemia reperfusion injury of the lung using an in vivo rat model. We administered MdNM (30mg/kg) or saline i.v. We clamped the left lung hilus for 60 min and then reperfused it for 60 min. We measured baseline arterial oxygen tension and calculated the percent recovery of the oxygen tension every 10 min during reperfusion. The percent recovery of oxygen tension was significantly higher ($p<0.05$) in the MdNM group (n=6)

than in the control group (n=6) at the end of the 60 min of ischemia and during the initial 30 min of reperfusion. The oxygen tension was still higher in the MdNM group at the end of the 60-min reperfusion, but the difference was not significant. Preischemic treatment with MdNM had a partial but significant protective effect against ischemia reperfusion injury of the lung.

CC 1-9 (Pharmacology)

IT **Anti-ischemic agents**
(protective effect of N-Me-1-deoxynojirimycin on lung ischemia reperfusion injury)

IT **Ischemia**
(pulmonary; protective effect of N-Me-1-deoxynojirimycin on lung ischemia reperfusion injury)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2003:498488 CAPLUS

DOCUMENT NUMBER: 139:305758

TITLE: Enhanced expression of aquaporin 4 in human brain with infarction

AUTHOR(S): Aoki, Kazuko; Uchihara, Toshiki; Tsuchiya, Kuniaki; Nakamura, Ayako; **Ikeda, Kenji**; Wakayama, Yoshihiro

CORPORATE SOURCE: Department of Neuropathology, Tokyo Metropolitan Institute for Neuroscience, Fuchu, Tokyo, 183-8526, Japan

SOURCE: Acta Neuropathologica (2003), 106(2), 121-124
CODEN: ANPTAL; ISSN: 0001-6322

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of human brains with cerebral infarction obtained at autopsy were investigated to clarify the possible contribution of aquaporin 4 (AQP4) to the development of brain edema. The cellular localization of AQP4 and its relation to ischemic foci were examined with double-labeling immunohistochem. AQP4 immunoreactivity (IR) was more intense at the periphery of ischemic foci than at their center. Double-labeling study demonstrated that AQP4-IR was restricted to astrocytes and was localized to their entire processes, including their end feet facing the outer surface of capillaries. Moreover, AQP4-IR, detectable in the subpial and subependymal zone in the normal condition, was more intense in the vicinity of ischemic foci. The accumulation of AQP4-IR may reflect its participation in the development of brain edema in human brains by playing a role in the transport of water not only through blood vessel walls but also through pial and ependymal surface of the brain.

CC 14-10 (Mammalian Pathological Biochemistry)

IT Edema
Ischemia
(cerebral; enhanced expression of aquaporin 4 in astrocytes of human brain with infarction)

IT **Brain, disease**
(**ischemia**; enhanced expression of aquaporin 4 in astrocytes of human brain with infarction)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2003:623915 CAPLUS

DOCUMENT NUMBER: 140:53253
TITLE: Oral administration of a neuroprotective compound T-588 prevents motoneuron degeneration after facial nerve avulsion in adult rats
AUTHOR(S): **Ikeda, Ken**; Sakamoto, Tsuyoshi; Marubuchi, Shigeki; Kawazoe, Yoko; Terashima, Nobuo; Iwasaki, Yasuo; Kinoshita, Masao; Ono, Satoshi; Nakagawa, Masaya; Watabe, Kazuhiko
CORPORATE SOURCE: Department of Molecular Neuropathology, Tokyo Metropolitan Institute for Neuroscience, Tokyo, Japan
SOURCE: Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders (2003), 4(2), 74-80
CODEN: ALSCFA; ISSN: 1466-0822
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB R(-)-1-(benzo[b]thiophen-5-yl)2-[2-(N,N-diethylamino) ethoxy]ethanol hydrochloride (T-588), a synthetic compound, has been shown to have neuroprotective potentials for neuronal cells. We investigated whether orally administered T-588 can rescue injured motoneurons after facial nerve avulsion in adult rats. The right facial nerves of adult Fischer 344 male rats were avulsed and the animals were freely administered solution of 0.05% (w/v) T-588 or received T-588 (3-30 mg/kg/day) through an oral tube for 1-4 wk. Facial motoneurons on both sides of the facial nuclei were counted in Nissl-stained sections, and choline acetyl-transferase (ChAT) immunoreactivity in injured motoneurons and ChAT enzyme activities in the ventral brain stem tissue containing the facial nuclei were examined Both free oral administration of 0.05% T-588 solution and oral tube administration of T-588 (30 mg/kg/day) improved the survival of facial motoneurons at 3 or 4 wk after avulsion. These treatments ameliorated ChAT immunoreactivity in injured motoneurons and the tissue ChAT enzyme activities at 1-wk postoperation examined These results indicate that oral administration of T-588 ameliorates the survival of injured motoneurons and supports their neuronal function after facial nerve avulsion in adult rats. T-588 may have therapeutic potential in motoneuron injury or motor neuron diseases in humans.

CC 1-11 (Pharmacology)
IT **Cytoprotective agents**
(**neuroprotective**; oral administration **neuroprotective** compound T-588 prevents motoneuron degeneration after facial nerve avulsion)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 16 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2004052417 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14753402
TITLE: PET neuroreceptor imaging as predictor of severe cerebral **ischemic** insult.
AUTHOR: Nariai T; Shimada Y; Ishiwata K; Nagaoka T; **Shimada J**; Kuroiwa T; Ono K I; Hirakawa K; Senda M; Óhno K
CORPORATE SOURCE: Department of Neurosurgery, Tokyo Medical and Dental University, Japan.. nariai.nsrg@tmd.ac.jp
SOURCE: Acta neurochirurgica. Supplement, (2003) 86 45-8.
Journal code: 100962752. ISSN: 0065-1419.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040203
Last Updated on STN: 20040310
Entered Medline: 20040309

AB Measurement of the adenosine A1 receptor (A1-R) with positron emission tomography (PET) using a newly developed positron ligand, [1-methyl-11C]8-dicyclopropylmethyl-1-methyl-3-propylxanthine (MPDX). were performed in a cat middle cerebral artery (MCA) occlusion and reperfusion. Eighteen adult cats underwent PET measurement of; 1) cerebral blood flow (CBF). 2) A1-R, 3) central benzodiazepine receptor (BDZ-R) and 4) glucose metabolism with 15O labeled water, MPDX, 11C-flumazenil (FMZ) and 18F-fluorodeoxyglucose (FDG), respectively. The CBF, A1-R, BDZ-R and FDG uptake were serially measured after 60 min occlusion of MCA in this order. MPDX binding and FMZ binding, but not CBF and FDG uptake, were significantly reduced in the groups with severer **ischemic** insult than in the groups with no or milder insults. Of the two receptor ligands, the reduction rate of the MPDX binding to A1-Rs was larger in a group that caused fatal **ischemic** insult. The newly developed PET in vivo imaging technique using MPDX was suitable in evaluating the function of adenosine and A1-Rs in relation to cerebral **ischemia**

CT Animals
*Brain: ME, metabolism
*Brain: RI, radionuclide imaging
Brain Ischemia: ME, metabolism
Brain Ischemia: MO, mortality
***Brain Ischemia: PP, physiopathology**
***Brain Ischemia: RI, radionuclide imaging**
Cats
Cerebrovascular Circulation
Contrast Media: ME, metabolism
Flumazenil: ME, metabolism
Fluorodeoxyglucose F18: PK, pharmacokinetics
Ligands
Prognosis
Receptor, Adenosine A1: ME, metabolism
Receptors, GABA-A: ME, metabolism
*Receptors, Sensory: ME, metabolism
Severity of Illness Index
Tomography, Emission-Computed
Xanthines: ME, metabolism

RN 63503-12-8 (Fluorodeoxyglucose F18); 78755-81-4 (Flumazenil)
CN 0 (1-methyl-8-dicyclopropylmethyl-1-methyl-3-propylxanthine); 0 (Contrast Media); 0 (Ligands); 0 (Receptor, Adenosine A1); 0 (Receptors, GABA-A); 0 (Xanthines)

L92 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2002:851689 CAPLUS
DOCUMENT NUMBER: 138:117933
TITLE: Protective effect of interleukin-3 and erythropoietin on motor neuron death after neonatal axotomy
AUTHOR(S): Iwasaki, Yasuo; **Ikeda, Ken**; Ichikawa, Yasumitsu; Igarashi, Osamu; Iwamoto, Kounosuke; Kinoshita, Masao
CORPORATE SOURCE: The Fourth Department of Internal Medicine, Toho University Ohashi Hospital, Tokyo, Japan
SOURCE: Neurological Research (2002), 24(7), 643-646
CODEN: NRESDZ; ISSN: 0161-6412
PUBLISHER: Forefront Publishing

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several members of hematopoietic factors are known to have neuroprotective effects against axotomized motor neuron death. The authors carried out a study to determine whether interleukin-3 (IL-3) and erythropoietin (EPO) rescue spinal motor neuron death following axotomy. Unilateral sciatic nerve was transected in neonatal rats. Different doses of IL-3, EPO, or vehicle were administered daily for two weeks by i.p. injection. After treatment, the number of spinal motor neurons was determined at the level of L4 segment. In comparison with vehicle, both IL-3 (10 μg kg-1) and EPO (5.0 mg kg-1) significantly prevented the loss of motor neurons. Protective potentials is the same between them. These results suggest that IL-3 and EPO play a role for motor neuron survival in vivo and suggest the potential use of these hematopoietic factors in treating diseases that involve degeneration and death of motor neurons, such as motor neuropathy and amyotrophic lateral sclerosis.
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 14
IT **Cytoprotective agents**
(**neuroprotective**; interleukin-3 and erythropoietin protective effect on spinal motor neuron death after neonatal axotomy)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2002:780609 CAPLUS
DOCUMENT NUMBER: 138:331558
TITLE: Neuroprotective actions of FK506 and cyclosporin A on motor neuron survival following neonatal axotomy
AUTHOR(S): Iwasaki, Yasuo; Ichikawa, Yasumitsu; Igarashi, Osamu; Iwamoto, Kounosuke; Kinoshitata, Masao; **Ikeda, Ken**
CORPORATE SOURCE: The Fourth Department of Internal Medicine, Toho University Ohashi Hospital, Tokyo, Japan
SOURCE: Neurological Research (2002), 24(6), 573-576
CODEN: NRESDZ; ISSN: 0161-6412
PUBLISHER: Forefront Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We show that non-immunosuppressive analogs of the immunosuppressive drugs FK506 and cyclosporin A (CsA) rescue axotomized neonatal motor neuron death. Unilateral sciatic nerve was transected in neonatal rats. Animals were then treated daily with different doses of FK506 and CsA for 14 days with i.p. injection. Control rats received phosphate buffer saline (PBS) in the same fashion. After treatment, the number of spinal motor neurons was determined at L4 level. In comparison with vehicle, both FK506 (5.0 mg kg-1) and CsA (10.0 mg kg-1) rescued motor neuron death in a similar way. These results indicate therapeutic relevance in the treatment of damaged motor neuron disorders, such as motor neuropathy or amyotrophic lateral sclerosis.
CC 1-11 (Pharmacology)
IT **Cytoprotective agents**
(**neuroprotective**; **neuroprotective** actions of FK506 and cyclosporin A on motor neuron survival following neonatal axotomy)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 19 OF 47 MEDLINE on STN

ACCESSION NUMBER: 2003247299 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12769603
TITLE: Molecular and cellular mechanism of glutamate receptors in relation to amyotrophic lateral sclerosis.
AUTHOR: Iwasaki Yasuo; **Ikeda Ken**; Kinoshita Masao
CORPORATE SOURCE: Fourth Department of Internal Medicine, Toho University Ohashi Hospital, 2-17-6, Ohashi, Meguro-ku, Tokyo 153-8515, Japan.. yaso@med.toho-u.ac.jp
SOURCE: Current drug targets. CNS and neurological disorders, (2002 Oct) 1 (5) 511-8. Ref: 78
Journal code: 101151150. ISSN: 1568-007X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030529
Last Updated on STN: 20030618
Entered Medline: 20030617

AB Amyotrophic lateral sclerosis (ALS) is a fatal **neurodegenerative** disorder of the central nervous system (CNS) with an unknown etiology. This disorder is characterized clinically by muscular weakness and wasting, and pathologically by selective degeneration of the corticospinal tracts and motor neurons of the brain stem and spinal cord. Median survival following onset is 3 to 5 years. Riluzole, an antiglutamatergic agent has been shown to have modest beneficial effects on survival. Glutamate is the main excitatory neurotransmitter in the CNS and excessive activation of glutamate receptors is excitotoxic to neurons. Glutamate receptor-mediated excitotoxicity has been proposed to explain the pattern of selective neuronal cell death and clinical manifestation of ALS. Activation of glutamate receptors leading to elevation of intracellular calcium may play a major role. This review will focus on the current understanding of the molecular and cellular mechanisms of glutamate receptors in relation to ALS.

CT *Amyotrophic Lateral Sclerosis: DT, drug therapy
*Amyotrophic Lateral Sclerosis: ME, metabolism
Animals
Binding Sites: DE, drug effects
Binding Sites: PH, physiology
Excitatory Amino Acid Antagonists: PD, pharmacology
Excitatory Amino Acid Antagonists: TU, therapeutic use
Glutamic Acid: ME, metabolism
Humans
*Receptors, Glutamate: ME, metabolism

RN 56-86-0 (Glutamic Acid)
CN 0 (Excitatory Amino Acid Antagonists); 0 (Receptors, Glutamate)

L92 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2002:579271 CAPLUS
DOCUMENT NUMBER: 138:130974
TITLE: Trophic effect of olmesartan, a novel AT1R antagonist, on spinal motor neurons in vitro and in vivo
AUTHOR(S): Iwasaki, Yasuo; Ichikawa, Yasumitsu; Igarashi, Osamu; Kinoshita, Masao; **Ikeda, Ken**
CORPORATE SOURCE: Fourth Department of Internal Medicine, Toho University Ohashi Hospital, Tokyo, Japan
SOURCE: Neurological Research (2002), 24(5), 468-472

CODEN: NRESDZ; ISSN: 0161-6412
PUBLISHER: Forefront Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Olmesartan is a novel compound which was shown to exhibit various neuropharmacol. effects. For the purpose of clarifying the effect of olmesartan on spinal motor neurons, the authors studied the following tests. The authors studied the effect in vitro of olmesartan on neurite outgrowth and choline acetyltransferase (ChAT) activity in primary explant cultures of ventral spinal cord (VSCC) of fetal rats. Olmesartan-treated VSCC, compared with control VSCC, had a significant neurite outgrowth and increased activity of ChAT. The effect was dose-related in neurite outgrowth. However, there was no relationship between activity of ChAT and given doses of olmesartan. The authors examined in vivo the effect of olmesartan on axotomized spinal motor neuron death in the rat spinal cord. After post-natal unilateral section of sciatic nerve, there was approx. a 50% survival of motor neurons, in the 4th lumbar segment. In comparison with vehicle, i.p. injection of olmesartan for consecutive 14 days reduced spinal motor neuron death. There was no relationship between number of surviving neurons and doses of olmesartan. These in vitro and in vivo studies showed that olmesartan has a neurotrophic effect on spinal motor neurons. The authors' data suggest a potential therapeutic use of olmesartan in treating diseases that involve degeneration and death of motor neurons, such as motor neuropathy and amyotrophic lateral sclerosis.
CC 1-11 (Pharmacology)
IT **Cytoprotective agents**
(neuroprotective; neurotrophic effect of olmesartan on spinal motor neurons in vitro and in vivo)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 21 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2003371027 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12849392
TITLE: Global democratic consensus on neuropathological disease criteria.
AUTHOR: Achim Cristian; Auer Roland; Bergeron Catherine; Cardozo Adriana; Deprez Manuel; de Vos Rob; Duyckaerts Charles; Egensperger Rupert; Esiri Margaret; Frosch Matthew P; Giannini Caterina; Goebel Hans H; Graeber Manuel B; Graham David I; Gray Francoise; Haltia Matti; Hashizume Yoshio; **Ikeda Kenji**; Ironside James W; Kreutzberg Georg W; Lantos Peter; Lowe James; Ludwin Samuel; Matsumoto Yoh; Olsson Yngve; Sasaki Atsushi; Scheithauer Bernd W; Takahashi Hitoshi; Tolnay Markus; Trojanowski John Q; Troost Dirk; de F Webster Henry
SOURCE: Lancet. Neurology, (2002 Oct) 1 (6) 340.
Journal code: 101139309. ISSN: 1474-4422.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030809
Last Updated on STN: 20030829
Entered Medline: 20030828
CT Brain Neoplasms: CL, classification
Brain Neoplasms: PA, pathology
Humans

*Nervous System Diseases: CL, classification
Nervous System Diseases: PA, pathology
Neurodegenerative Diseases: CL, classification
Neurodegenerative Diseases: PA, pathology
*Neurology: ST, standards
Phenotype
Terminology

L92 ANSWER 22 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2002442218 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12200618
TITLE: NACP/alpha-synuclein immunoreactivity in diffuse neurofibrillary tangles with calcification (DNTC).
AUTHOR: Yokota Osamu; Terada Seishi; Ishizu Hideki; Tsuchiya Kuniaki; Kitamura Yoshihiro; **Ikeda Kenji**; Ueda Kenji; Kuroda Shigetoshi
CORPORATE SOURCE: Department of Neuropsychiatry, Okayama University Graduate School of Medicine and Dentistry, 2-5-1 Shikata-cho, Okayama 700-8558, Japan.. terada_1@cc.okayama-u.ac.jp
SOURCE: Acta neuropathologica, (2002 Oct) 104 (4) 333-41. Electronic Publication: 2002-05-08. Journal code: 0412041. ISSN: 0001-6322.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020830
Last Updated on STN: 20030105
Entered Medline: 20021227

AB Diffuse neurofibrillary tangles with calcification (DNTC) is a rare tangle-predominant dementia, as well as one of the tauopathies lacking Abeta deposition. It is characterized by temporo-frontal lobar atrophy, Fahr-type calcification and, histopathologically, numerous neurofibrillary tangles in the limbic system and neocortex. Recently, accumulation of alpha-synuclein (alphaS), the precursor of the non-beta amyloid component (NAC) of Alzheimer's disease, has been shown in diverse **neurodegenerative** disorders, including Parkinson's disease, dementia with Lewy bodies, Alzheimer's disease, multiple system atrophy and parkinsonism-dementia complex of Guam. To clarify whether alphaS accumulates in other **neurodegenerative** disorders, we investigated eight DNTC brains using immunohistochemistry and demonstrated remarkable alphaS deposition in the neurons and astrocytes in many anatomical regions. Abundant Lewy bodies were observed in the amygdala (seven cases) and hippocampus (seven cases), and, to a lesser degree, in the substantia nigra (six cases) and dorsal vagal nucleus (five cases). In the hippocampus, many Lewy neurites were distributed in the stratum oriens and stratum pyramidale in the CA2-3 and the subiculum. Furthermore, numerous NAC-positive astrocytes were detected in the hippocampus and temporal cortex. This investigation reveals that neurons and astrocytes are extensively involved in remarkable alphaS pathology in the DNTC brain, and that the alphaS pathology compounds the cardinal pathological features of tau pathology. These findings suggest that (1) DNTC shares a common pathophysiological background with Parkinson's disease, dementia with Lewy bodies, and multiple system atrophy in which abnormal alphaS aggregation is observed, and (2) there is an interaction between alphaS and tau pathology that does not involve amyloid in DNTC.

CT Check Tags: Comparative Study; Female; Male
Adult

Aged
Amyloid: ME, metabolism
Astrocytes: ME, metabolism
Brain: ME, metabolism
Brain: PA, pathology
*Calcinosis: ME, metabolism
Calcinosis: PA, pathology
*Dementia: ME, metabolism
Dementia: PA, pathology
Humans
Immunohistochemistry
Lewy Bodies: PA, pathology
Middle Aged
*Nerve Tissue Proteins: ME, metabolism
*Neurofibrillary Tangles: ME, metabolism
Neurofibrillary Tangles: PA, pathology
Neurons: ME, metabolism
Research Support, Non-U.S. Gov't
Ubiquitin: ME, metabolism
tau Proteins: ME, metabolism
RN 119938-65-7 (synuclein)
CN 0 (Amyloid); 0 (Nerve Tissue Proteins); 0 (Ubiquitin); 0 (tau Proteins)

L92 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 2002:385987 CAPLUS
DOCUMENT NUMBER: 137:345943
TITLE: Intracerebral adenosine infusion improves neurological outcome after transient focal ischemia in rats
AUTHOR(S): Kitagawa, Hisashi; Mori, Atsushi; **Shimada, Jun** ; Mitsumoto, Yasuhide; Kikuchi, Tetsuro
CORPORATE SOURCE: Second Institute of New Drug Research, Otsuka Pharmaceutical Co., Ltd, Tokushima, 771-0192, Japan
SOURCE: Neurological Research (2002), 24(3), 317-323
CODEN: NRESDZ; ISSN: 0161-6412
PUBLISHER: Forefront Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to elucidate the role of adenosine in brain ischemia, the possible protective effects of adenosine on ischemic brain injury were investigated in a rat model of brain ischemia both in vitro and in vivo. Exogenous adenosine dose-dependently rescued cortical neuronal cells from injury after glucose deprivation in vitro. Adenosine (1 mM) also significantly reduced hypoglycemia/hypoxia-induced glutamate release from the hippocampal slice. In a rat model of transient middle cerebral artery occlusion (MCAO), extracellular adenosine concentration was increased immediately after occlusion, and then returned to the baseline by 30 min after reperfusion. Adenosine infusion through a microdialysis probe into the ipsilateral striatum (1 mM adenosine, 2 μL min-1, total 4.5 h from the occlusion to 3 h after reperfusion) showed a significant improvement in the neurol. outcome, and .apprx.25% reduction of infarct volume, although the effect did not reach statistical significance, compared with the vehicle-treated group at 20 h after 90 min of MCAO. These results demonstrated the neuroprotective effect of adenosine against ischemic brain injury both in vitro and in vivo, suggesting the possible therapeutic application of adenosine regulating agents, which inhibit adenosine uptake or metabolism to enhance or maintain extracellular endogenous adenosine levels, for stroke treatment.
CC 1-11 (Pharmacology)

Section cross-reference(s): 14
IT **Ischemia**
(cerebral; intracerebral adenosine infusion improves neurol. outcome after transient focal ischemia)
IT **Brain**
(hippocampus; adenosine effect on hypoglycemia/hypoxia-induced glutamate release from hippocampus in relation to neurol. outcome after transient focal **ischemia**)
IT **Brain, disease**
(**ischemia**; intracerebral adenosine infusion improves neurol. outcome after transient focal **ischemia**)
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 24 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2002170078 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11902116
TITLE: **Neuroprotection** by adenosine A2A receptor blockade in experimental models of Parkinson's disease.
AUTHOR: **Ikeda Ken**; **Kurokawa Masako**; Aoyama Shiro; **Kuwana Yoshihisa**
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Co, Ltd, Nagaizumi, Sunto, Shizuoka, Japan.
SOURCE: Journal of neurochemistry, (2002 Jan) 80 (2) 262-70. Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020321
Last Updated on STN: 20020405
Entered Medline: 20020404
AB Adenosine A2A receptors are abundant in the caudate-putamen and involved in the motor control in several species. In MPTP-treated monkeys, A2A receptor-blockade with an antagonist alleviates parkinsonian symptoms without provoking dyskinesia, suggesting this receptor may offer a new target for the antisymptomatic therapy of Parkinson's disease. In the present study, a significant **neuroprotective** effect of A2A receptor antagonists is shown in experimental models of Parkinson's disease. Oral administration of A2A receptor antagonists protected against the loss of nigral dopaminergic neuronal cells induced by 6-hydroxydopamine in rats. A2A antagonists also prevented the functional loss of dopaminergic nerve terminals in the striatum and the ensuing gliosis caused by MPTP in mice. The **neuroprotective** property of A2A receptor antagonists may be exerted by altering the packaging of these neurotoxins into vesicles, thus reducing their effective intracellular concentration. We therefore conclude that the adenosine A2A receptor may provide a novel target for the long-term medication of Parkinson's disease, because blockade of this receptor exerts both acutely antisymptomatic and chronically **neuroprotective** activities.
CT Check Tags: Male
1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine
1-Methyl-4-phenylpyridinium: PK, pharmacokinetics
Animals
Antineoplastic Agents: PD, pharmacology
Disease Models, Animal
Dopamine: PK, pharmacokinetics
Dopamine Agents

Gliosis: DT, drug therapy
Gliosis: PC, prevention & control
Herbicides: PK, pharmacokinetics
Nerve Degeneration: DT, drug therapy
Neurons: CY, cytology
Neurons: DE, drug effects
Neurons: ME, metabolism
***Neuroprotective Agents: PD, pharmacology**
Oxidopamine
PC12 Cells
Parkinsonian Disorders: CI, chemically induced
*Parkinsonian Disorders: DT, drug therapy
*Purines: PD, pharmacology
Rats
Rats, Sprague-Dawley
Receptor, Adenosine A2A
*Receptors, Purinergic P1: AI, antagonists & inhibitors
Sympatholytics
Tritium: DU, diagnostic use

RN 10028-17-8 (Tritium); 1199-18-4 (Oxidopamine); 155270-99-8 (istradefylline); 28289-54-5 (1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine); 48134-75-4 (1-Methyl-4-phenylpyridinium); 51-61-6 (Dopamine)

CN 0 (Antineoplastic Agents); 0 (Dopamine Agents); 0 (Herbicides); 0 (**Neuroprotective** Agents); 0 (Purines); 0 (Receptor, Adenosine A2A); 0 (Receptors, Purinergic P1); 0 (Sympatholytics)

L92 ANSWER 25 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2002290426 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12030417
TITLE: Demonstration and distribution of tau-positive glial coiled body-like structures in white matter and white matter threads in early onset Alzheimer's disease.
AUTHOR: Umahara Takahiko; Tsuchiya Kuniaki; **Ikeda Kenzi**; Kanaya Kiyoshi; Iwamoto Toshihiko; Takasaki Masharu; Mukai Kiyoshi; Shibata Noriyuki; Kato Shinsuke
CORPORATE SOURCE: Department of Geriatrics, Tokyo Medical University, Japan.. takahiko@tokyo-med.ac.jp
SOURCE: Neuropathology : official journal of the Japanese Society of Neuropathology, (2002 Mar) 22 (1) 9-12. Journal code: 9606526. ISSN: 0919-6544.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20020528
Last Updated on STN: 20021214
Entered Medline: 20021127

AB The present report concerns the demonstration and distribution of tau-positive structures in the frontal and temporal white matter of five autopsy cases of early onset Alzheimer's disease (AD). The relationship between white matter lesions and tau positive structures was also investigated. Five early onset AD brains, which had not only unambiguous white matter lesions, but also no or rare atherosclerosis and minimal amyloid angiopathy, were examined. There were several tau-positive coiled body-like structures and many thread-like structures in the white matter, although previous reports showed only a few coiled bodies in the white matter in the AD brain. No relationship was found between the degree of

each white matter lesion and number or distribution of tau-positive structures in the white matter. The results suggest that the AD brain has tau-positive structures in the white matter similar to some **neurodegenarative** brain diseases such as progressive supranuclear palsy, corticobasal degeneration, and dementia with grains. However, tau abnormalities may have fewer effects when they are located in white matter lesions in AD.

CT Age of Onset
*Alzheimer Disease: PA, pathology
Brain: PA, pathology
Humans
*Inclusion Bodies: CH, chemistry
Inclusion Bodies: PA, pathology
Middle Aged
Neurofibrillary Tangles: CH, chemistry
Neurofibrillary Tangles: PA, pathology
*Neuroglia: CH, chemistry
*Neuroglia: PA, pathology
*tau Proteins: AN, analysis
CN 0 (tau Proteins)

L92 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 2001:114077 CAPLUS
DOCUMENT NUMBER: 134:293974
TITLE: Endogenously released DOPA is a causal factor for glutamate release and resultant delayed neuronal cell death by transient ischemia in rat striata
AUTHOR(S): Furukawa, Nobuya; Arai, Nobutaka; Goshima, Yoshio; Miyamae, Takeaki; Ohshima, Etsuo; **Suzuki, Fumio**; Fujita, Kiyohide; Misu, Yoshimi
CORPORATE SOURCE: Department of Pharmacology, Department Oral and Maxillofacial Surgery, Yokohama City University School of Medicine, Yokohama, 236-0004, Japan
SOURCE: Journal of Neurochemistry (2001), 76(3), 815-824
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glutamate is implicated in neuronal cell death. Exogenously applied DOPA by itself releases neuronal glutamate and causes neuronal cell death in in vitro striatal systems. Herein, we attempt to clarify whether endogenous DOPA is released by 10 min transient ischemia due to four-vessel occlusion during rat striatal microdialysis and, further, whether DOPA, when released, functions to cause glutamate release and resultant delayed neuronal cell death. Ischemia increased extracellular DOPA, dopamine, and glutamate, and elicited neuronal cell death 96 h after ischemic insult. Inhibition of striatal L-aromatic amino acid decarboxylase 10 min before ischemia increased markedly basal DOPA, tripled glutamate release with a tendency of decrease in dopamine release by ischemia, and exaggerated neuronal cell death. Intrastriatal perfusion of 10-30 nM DOPA cyclohexyl ester, a competitive DOPA antagonist, 10 min before ischemia, concentration-dependently decreased glutamate release without modification of dopamine release by ischemia. At 100 nM, the antagonist elicited a slight ceiling effect on decreases in glutamate release by ischemia and protected neurons from cell death. Glutamate was released concentration-dependently by intrastriatal perfusion of 0.3-1 mM DOPA and stereoselectively by 0.6 mM DOPA. The antagonist elicited no hypothermia during and after ischemia. Endogenously released DOPA is an upstream causal factor for glutamate release and resultant delayed neuronal cell death by brain ischemia in rat

striata. DOPA antagonist has a neuroprotective action.
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
IT **Nerve, disease**
(death; DOPA release is a causal factor for glutamate release and resultant delayed neuronal cell death by transient **ischemia** in rat striatum)
IT **Brain**
(hippocampus; DOPA release is a causal factor for glutamate release and resultant delayed neuronal cell death by transient **ischemia** in rat striatum)
IT **Brain, disease**
(**striatum**, **ischemia**, **transient**; DOPA release is a causal factor for glutamate release and resultant delayed neuronal cell death by transient **ischemia** in rat striatum)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 2001:95796 CAPLUS
DOCUMENT NUMBER: 135:40861
TITLE: DOPA cyclohexyl ester, a competitive DOPA antagonist, protects glutamate release and resultant delayed neuron death by transient ischemia in hippocampus CA1 of conscious rats
AUTHOR(S): Arai, N.; Furukawa, N.; Miyamae, T.; Goshima, Y.; Sasaki, Y.; Ohshima, E.; **Suzuki, F.**; Fujita, K.; Misu, Y.
CORPORATE SOURCE: Department of Clinical Neuropathology, Tokyo Metropolitan Institute of Neuroscience, Tokyo, 183-8526, Japan
SOURCE: Neuroscience Letters (2001), 299(3), 213-216
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In rat striata, DOPA released is a causal factor for glutamate release and resultant delayed neuron death by four-vessel occlusion. Nanomolar DOPA cyclohexyl ester (CHE), a potent and relatively stable competitive DOPA antagonist, protects these events. We tried to clarify whether DOPA CHE protects these events in hippocampal CA1 pyramidal cell layers most vulnerable against ischemia. Five to 10 min ischemia caused slight to mild glutamate release in 10 min samples during microdialysis and mild to severe neuron death 96 h after reperfusion. DOPA and dopamine were under assay limit in this design, but were basally detected by 20 min sampling and released by 20 min ischemia. In 10 min samples, intrahippocampal perfusion of 100 nM DOPA CHE 10 min before ischemia for 70 min did not inhibit glutamate release by 10 min ischemia, while it abolished glutamate release and protected delayed neuron death by 5 min ischemia. DOPA CHE is neuroprotective under a mild ischemic condition in rat hippocampus CA1.
CC 1-11 (Pharmacology)
IT **Anti-ischemic agents**
(DOPA cyclohexyl ester, a competitive DOPA antagonist, protects glutamate release and resultant delayed neuron death by transient ischemia in hippocampus CA1 of conscious rats)
IT **Nerve, disease**
(death; DOPA cyclohexyl ester, a competitive DOPA antagonist, protects glutamate release and resultant delayed neuron death by transient **ischemia** in hippocampus CA1 of conscious rats)

IT **Brain**
(hippocampus, sector CA1, pyramidal cell layer; DOPA cyclohexyl ester, a competitive DOPA antagonist, protects glutamate release and resultant delayed neuron death by transient **ischemia** in hippocampus CA1 of conscious rats)
IT **Cytoprotective agents**
(**neuroprotectants**; DOPA cyclohexyl ester, a competitive DOPA antagonist, protects glutamate release and resultant delayed neuron death by transient ischemia in hippocampus CA1 of conscious rats)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 28 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2001116419 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11068135
TITLE: Long-term increase of GluR2 alpha-amino-3-hydroxy-5-methylisoxazole-4-propionate receptor subunit in the dispersed dentate gyrus after intrahippocampal kainate injection in the mouse.
AUTHOR: **Suzuki F**; Hirai H; Onteniente B; Riban V; Matsuda M; Kurokawa K
CORPORATE SOURCE: Department of Neurosurgery and Anatomy, Shiga University of Medical Science, Seta-Tsukinowa-cho, Ohtsu, Shiga 520-2192, Japan.. fsuzuki@belle.shiga-med.ac.jp
SOURCE: Neuroscience, (2000) 101 (1) 41-50.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

AB Intrahippocampal injection of a subtoxic dose of kainate in mice has been shown to induce a dispersion of granule cells of the dentate gyrus, which is a characteristic morphological change often seen in human hippocampal sclerosis. In addition, it has been shown recently that such injections lead to recurrent hippocampal seizures and changes in glucose metabolism, which are reminiscent of temporal lobe epilepsy. Previous reports on human hippocampal sclerosis have shown an increase of the expression of the GluR2 alpha-amino-3-hydroxy-5-methylisoxazole-4-propionate subunits in the dispersed granule cell somata. However, no such changes have been observed so far in animal models of epilepsy with hippocampal sclerosis. In this study, the expression of alpha-amino-3-hydroxy-5-methylisoxazole-4-propionate receptor subunits was examined by immunohistochemistry following intrahippocampal injection of kainate in mice and rats. In mice, such injection induced a persistent increase of GluR2 immunoreactivity in the granule cells for up to 180 days. By contrast, GluR1 immunoreactivity was transiently increased during the first four days after the injection and progressively decreased thereafter. By contrast, intrahippocampal injection of kainate in rats did not result in granule cell dispersion and no changes in GluR1 immunoreactivity or GluR2 immunoreactivity were observed.These results show that, in addition to morphological, clinical and metabolical similarities, intrahippocampal injection of kainate results in a persistent increase of GluR2 associated with granule cell dispersion, as in human hippocampal sclerosis. These data suggest the existence of common mechanisms between granule cell dispersion and regulation of GluR2 subunits associated with hippocampal

sclerosis.
CT Animals
Dentate Gyrus: DE, drug effects
*Dentate Gyrus: ME, metabolism
Dentate Gyrus: PA, pathology
Disease Models, Animal
Epilepsy: ME, metabolism
Epilepsy: PA, pathology
Epilepsy: PP, physiopathology
*Kainic Acid: TO, toxicity
Mice
Mice, Inbred C57BL
Nerve Degeneration: CI, chemically induced
Nerve Degeneration: ME, metabolism
Nerve Degeneration: PA, pathology
Neurodegenerative Diseases: ME, metabolism
Neurodegenerative Diseases: PA, pathology
Neurodegenerative Diseases: PP, physiopathology
Neuronal Plasticity: PH, physiology
Neurons: DE, drug effects
*Neurons: ME, metabolism
Neurons: PA, pathology
Rats
Rats, Wistar
Receptors, AMPA: DE, drug effects
*Receptors, AMPA: ME, metabolism
Research Support, Non-U.S. Gov't
Time Factors
RN 487-79-6 (Kainic Acid)
CN 0 (AMPA receptor, GluR2 subunit); 0 (AMPA receptor, GluR3 subunit); 0 (AMPA receptor, GluR4); 0 (GluR1 protein); 0 (Receptors, AMPA)

L92 ANSWER 29 OF 47 MEDLINE on STN
ACCESSION NUMBER: 2001015763 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10874587
TITLE: L-DOPA cyclohexyl ester is a novel potent and relatively stable competitive antagonist against L-DOPA among several L-DOPA ester compounds.
AUTHOR: Furukawa N; Goshima Y; Miyamae T; Sugiyama Y; Shimizu M; Ohshima E; **Suzuki F**; Arai N; Fujita K; Misu Y
CORPORATE SOURCE: Department of Pharmacology, Yokohama City University School of Medicine, Japan.
SOURCE: Japanese journal of pharmacology, (2000 Jan) 82 (1) 40-7. Journal code: 2983305R. ISSN: 0021-5198.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001101
AB We explored L-DOPA esters with chemically bulky structures to find a potent stable competitive antagonist against L-DOPA, compared to DOPA methyl ester (DOPA ME). In anesthetized rats, DOPA cyclohexyl ester (DOPA CHE), DOPA cyclopentyl ester (DOPA CPE) and DOPA cyclopentyldimethyl ester (DOPA CPDME) at 1 microgram microinjected into depressor sites of the nucleus tractus solitarii elicited or tended to elicit more marked antagonism against depressor responses to 60 ng L-DOPA, compared to DOPA

ME. At 100 ng, DOPA CHE elicited the most potent antagonism. At 1 microgram, duration of the antagonistic activity of DOPA CHE was approximately three times longer than that of DOPA ME. During microdialysis of the nucleus accumbens, conversion from DOPA CHE at 1 microM perfused via probes to extracellular L-DOPA was the lowest among these compounds and less than one half of that from DOPA ME. Binding studies showed that the recognition site for L-DOPA differs from ionotropic glutamatergic, dopaminergic D1 and D2 receptors. We recently found that L-DOPA evoked by transient **ischemia** may act as a DOPA CHE-sensitive causal factor for glutamate release and resultant neuronal cell death. DOPA CHE is the most potent, relatively stable competitive antagonist against L-DOPA and is a useful mother compound to develop **neuroprotective** drugs.

CT Check Tags: Male
Animals
Binding, Competitive
Blood Pressure: DE, drug effects
Glutamic Acid: SE, secretion
Heart Rate: DE, drug effects
*Levodopa: AI, antagonists & inhibitors
Microdialysis
Microinjections
***Neuroprotective Agents: PD, pharmacology**
Rats
Rats, Sprague-Dawley
Rats, Wistar
Research Support, Non-U.S. Gov't

RN 56-86-0 (Glutamic Acid)
CN 0 (Levodopa); 0 (**Neuroprotective** Agents)

L92 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:194000 CAPLUS
DOCUMENT NUMBER: 130:218320
TITLE: Therapeutic agent for neural degeneration
INVENTOR(S): **Shimada, Junichi**; **Kurokawa, Masako**; **Ikeda, Ken**; Susuki, Fumio; **Kuwana, Yoshihisa**
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912546	A1	19990318	WO 1998-JP3980	19980904
W: AU, BG, BR, BY, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9889976	A1	19990329	AU 1998-89976	19980904
AU 734138	B2	20010607		
EP 1016407	A1	20000705	EP 1998-941725	19980904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2299909	AA	20010902	CA 2000-2299909	20000302
US 2003158214	A1	20030821	US 2000-486823	20000303

US 6727259	B2	20040427			
US 2004229888	A1	20041118	US 2003-692930		20031027
PRIORITY APPLN. INFO.:			JP 1997-240565	A	19970905
			WO 1998-JP3980	W	19980904
			US 2000-486823	A3	20000303

OTHER SOURCE(S): MARPAT 130:218320

AB Claimed are therapeutic agents for neural degeneration containing xanthine derivs. (Markush structure given). The bioactivity of (E)-1,3-diethyl-8-(3,4-dimethoxystyryl)-7-methylxanthine was demonstrated. Formulations containing compds. of this invention are given.

IC ICM A61K031-52
ICS C07D473-04; C07D473-20; C07D473-22

CC 1-11 (Pharmacology)
Section cross-reference(s): 63

IT **Cytoprotective agents**
(**neuroprotectants**; xanthine derivs. as therapeutic agents for neural degeneration)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 31 OF 47 MEDLINE on STN

ACCESSION NUMBER: 1999324072 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10394152
TITLE: The contribution of inducible nitric oxide and cytomegalovirus to the stability of complex carotid plaque.
AUTHOR: Hunter G C; Henderson A M; Westerband A; Kobayashi H; **Suzuki F**; Yan Z Q; Sirsjo A; Putnam C W; Hansson G K
CORPORATE SOURCE: Departments of Surgery, and Internal Medicine, The University of Texas Medical Branch, Galveston, TX, USA.
SOURCE: Journal of vascular surgery : official publication, Society for Vascular Surgery [and] International Society for Cardiovascular Surgery, North American Chapter, (1999 Jul) 30 (1) 36-49; discussion 50.
Journal code: 8407742. ISSN: 0741-5214.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 20000303
Entered Medline: 19990804

AB BACKGROUND: Although the association between inflammation and atherosclerosis is well established, the biologic events that trigger the local inflammatory response within plaque are not fully understood. Cytotoxic free radicals and infectious agents, both of which are associated with an inflammatory response, have previously been implicated in the initiation and progression of atherosclerosis. In this study, we analyzed carotid plaque for evidence of oxidative vascular injury by determining the presence and distribution of inducible nitric oxide synthase (iNOS) expression and nitrotyrosine formation and for evidence of infection with cytomegalovirus. METHODS: Carotid plaque from 51 patients who underwent endarterectomy for either primary (n = 37) or recurrent (n = 14) stenosis were examined histologically (hematoxylin-eosin staining and Masson's trichrome staining) and with immunohistochemistry with specific antibodies to alpha-smooth muscle actin, macrophages (CD68), T-lymphocytes (CD3), and T-cell activation (human leukocyte antigen-DR). Twenty-eight specimens from patients with primary (n = 15) and recurrent (n = 13)

stenosis were examined for the presence of iNOS and nitrotyrosine with immunohistochemistry and in situ hybridization (iNOS). Twenty-three additional specimens (22 primary, and 1 recurrent) were analyzed with antibodies to p53, cytomegalovirus, and the polymerase chain reaction (cytomegalovirus, n = 8). RESULTS: Primary atherosclerotic lesions were either complex heterogenous cellular plaques (n = 29) or relatively acellular fibrous plaques (n = 8). Ten of 14 recurrent plaques were either complex or fibrous lesions, and the remaining four were typical of myointimal thickening. CD68-positive staining cells were detected in all specimens regardless of their structural morphology. CD3-positive cells were interspersed between macrophages in all heterogeneous cellular plaques and only infrequently noted in fibrous plaques. iNOS and nitrotyrosine immunoreactivity were detected in macrophages and smooth muscle cells in all complex and fibrous plaques and in two of four myointimal plaques. The presence of iNOS and nitrotyrosine in plaque correlated with the existence of symptoms in 80% of primary and 62% of recurrent lesions. Cytomegalovirus was detected in only two of 23 carotid specimens (9%). CONCLUSION: The association between **ischemic** cerebrovascular symptoms and iNOS and nitrotyrosine immunoreactivity in complex primary and recurrent carotid plaque and the infrequent occurrence of cytomegalovirus in primary carotid lesions suggests that ongoing free radical oxidative damage rather than viral infection may contribute to plaque instability in patients with complex and fibrous carotid plaques.

CT Check Tags: Female; Male
Aged
Carotid Arteries: CH, chemistry
Carotid Arteries: PA, pathology
Carotid Stenosis: ME, metabolism
*Carotid Stenosis: PA, pathology
Carotid Stenosis: VI, virology
*Cytomegalovirus Infections: PA, pathology
Humans
Immunohistochemistry
In Situ Hybridization
Intracranial Arteriosclerosis: ME, metabolism
*Intracranial Arteriosclerosis: PA, pathology
Intracranial Arteriosclerosis: VI, virology
*Nitric-Oxide Synthase: ME, metabolism
Polymerase Chain Reaction
Recurrence
Research Support, U.S. Gov't, P.H.S.
Risk Factors
Tyrosine: AA, analogs & derivatives
Tyrosine: AN, analysis

RN 3604-79-3 (3-nitrotyrosine); 55520-40-6 (Tyrosine)

CN EC 1.14.13.39 (Nitric-Oxide Synthase); EC 1.14.13.39 (inducible nitric oxide synthase)

L92 ANSWER 32 OF 47 MEDLINE on STN

ACCESSION NUMBER: 1998355461 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9692712

TITLE: Correlated long-term increase of brain-derived neurotrophic factor and Trk B proteins in enlarged granule cells of mouse hippocampus after kainic acid injection.

AUTHOR: Inoue T; Hirai H; Onteniente B; **Suzuki F**

CORPORATE SOURCE: Department of Neurosurgery, Shiga University of Medical Science, Otsu, Japan.

SOURCE: Neuroscience, (1998 Oct) 86 (3) 723-8.
Journal code: 7605074. ISSN: 0306-4522.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 20000303
Entered Medline: 19981029

AB Our previous studies have shown that a single injection of kainic acid into the dorsal hippocampus of adult mice resulted in hypertrophy of the dentate gyrus granule cells. This hypertrophy was correlated with a long-lasting increase of brain-derived neurotrophic factor messenger RNA, and prevented by anti-sense brain-derived neurotrophic factor oligonucleotide treatment. These results suggest that an increase of brain-derived neurotrophic factor messenger RNA may be a major trigger of granule cells enlargement. However, the level of messenger RNA of Trk B, the high-affinity receptor of brain-derived neurotrophic factor, was not increased significantly, raising the question of whether increased brain-derived neurotrophic factor messenger RNA level leads actually to an increased protein production. The objective of the present study was to examine this; changes in contents of brain-derived neurotrophic factor and TrkB protein were monitored by immunohistochemistry during kainic acid-induced hypertrophy. Results show that immunoreactivities of brain-derived neurotrophic factor and Trk B were present in enlarged granule cells. These immunoreactivities increased from two to 16 weeks after kainic acid injection and were maintained up to 12 months. Simultaneous increases of brain-derived neurotrophic factor messenger RNA and protein, and of TrkB protein were coupled tightly to the chronology of granule cell enlargement, suggesting that the action of brain-derived neurotrophic factor in the induction and maintenance of kainic acid-induced granule cells enlargement is likely to be mediated by TrkB. The discrepancy between the previously described lack of increase of TrkB messenger RNA and the herein observed increase of the protein further reveals the existence of translational regulations of the receptor messenger RNA.

CT Check Tags: Male
Animals
Brain-Derived Neurotrophic Factor: BI, biosynthesis
*Brain-Derived Neurotrophic Factor: GE, genetics
Hippocampus: DE, drug effects
*Hippocampus: ME, metabolism
Hippocampus: PA, pathology
Hypertrophy
*Kainic Acid: TO, toxicity
Mice
Mice, Inbred C57BL
Neurons: DE, drug effects
*Neurons: ME, metabolism
Neurons: PA, pathology
Neuroprotective Agents
RNA, Messenger: GE, genetics
Receptor Protein-Tyrosine Kinases: BI, biosynthesis
*Receptor Protein-Tyrosine Kinases: GE, genetics
Receptor, Ciliary Neurotrophic Factor
Receptors, Nerve Growth Factor: BI, biosynthesis
*Receptors, Nerve Growth Factor: GE, genetics
Time Factors
Transcription, Genetic: DE, drug effects
RN 487-79-6 (Kainic Acid)

CN 0 (Brain-Derived Neurotrophic Factor); 0 (**Neuroprotective** Agents); 0 (RNA, Messenger); 0 (Receptor, Ciliary Neurotrophic Factor); 0 (Receptors, Nerve Growth Factor); EC 2.7.1.112 (Receptor Protein-Tyrosine Kinases)

L92 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:397326 CAPLUS
DOCUMENT NUMBER: 129:131414
TITLE: JTP-2942, a novel thyrotropin-releasing hormone analog, protects against spinal motor neuron degeneration in the wobbler mouse
AUTHOR(S): **Ikeda, Ken**; Iwasaki, Yasuo; Kinoshita, Masao
CORPORATE SOURCE: The Fourth Department of Internal Medicine, Toho University Ohashi Hospital, Tokyo, 153-8515, Japan
SOURCE: Neuroscience Letters (1998), 250(1), 9-12
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB JTP-2942, a novel TSH-releasing hormone (TRH) analog, exhibits a strong acetylcholine release-enhancing effect in the rat hippocampus and frontal cortex. This mol. has a more powerful and prolonged action on cholinergic neurons than TRH. Here the authors studied whether JTP-2942 treatment can ameliorate motor dysfunction and spinal motor neuron degeneration in the wobbler mouse. After clin. diagnosis at postnatal age 3-4 wk, wobbler mice received i.p. injections of JTP-2942 (2 mg/kg per day) for 4 wk (long-term treatment) or 2 wk (short-term treatment), TRH (50 mg/kg per day) for 4 wk or vehicle in a blind fashion. Compared with the vehicle, long-term administration of JTP-2942 potentiated grip strength, attenuated muscle contractures in the forelimbs, reduced denervation muscle atrophy and protected spinal motor neurons. After cessation of JTP-2942 (short-term treatment), motor dysfunction deteriorated rapidly. Symptomatic and neuropathol. progression were not retarded in mice that received TRH or short-term JTP-2942 treatment. The authors' results indicate that JTP-2942 may have therapeutic potential for lower motor neuron disease or motor neuropathy.
CC 2-5 (Mammalian Hormones)
IT **Cytoprotective agents**
(**neuroprotectants**; JTP-2942 novel TSH-releasing hormone analog protects against spinal motor neuron degeneration in wobbler mouse)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:595065 CAPLUS
DOCUMENT NUMBER: 127:229542
TITLE: Bromocriptine prevents neuron damage following inhibition of superoxide dismutase in cultured ventral spinal cord neurons
AUTHOR(S): Iwasaki, Yasuo; **Ikeda, Ken**; Shiojima, Toshiya; Tagaya, Nozomu; Kobayashi, Tomoko; Kinoshita, Masao
CORPORATE SOURCE: Fourth Department of Internal Medicine, Toho University Ohashi Hospital, Tokyo, Japan
SOURCE: Neurological Research (1997), 19(4), 389-392
CODEN: NRESDZ; ISSN: 0161-6412
PUBLISHER: Forefront Publishing
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Rosen et al. have reported point mutations in the cytosolic Cu/Zn superoxide dismutase (SOD 1) gene in some families with familial amyotrophic lateral sclerosis (ALS). To determine whether decreased SOD activity could contribute to neuronal damage, rat embryo ventral spinal cord neurons were incubated with diethyldithiocarbamate (DDC), an inhibitor of SOD. There was a marked increase in neuronal damage in cultures exposed to DDC and this phenomenon was dose-related. In this paradigm, these deteriorative changes were prevented by bromocriptine. DDC-treated ventral spinal cord neurons provide an in vitro model of free radical neurotoxicity, indicating that bromocriptine has a neuroprotective effect against free radicals.
CC 1-11 (Pharmacology)
IT **Cytoprotective agents**
(**neuroprotectants; neuroprotective** activity of bromocriptine, α-tocopherol and ascorbate)

L92 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:335993 CAPLUS
DOCUMENT NUMBER: 127:29051
TITLE: Chlorpromazine inhibits concanavalin A-induced liver injury independently of cytokine modulation
AUTHOR(S): **Ikeda, Ken**; Hirano, Masako; Orita, Akiko; Takeuchi, Makoto
CORPORATE SOURCE: Infectious Disease Immunol. Res. Lab., Inst. Drug Discovery Res., Yamanouchi Pharm. co. Ltd., Tsukuba, 305, Japan
SOURCE: Immunology Letters (1997), 55(3), 127-131
CODEN: IMLED6; ISSN: 0165-2478
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the effect of chlorpromazine (CPZ) in a murine model of T-cell-dependent liver injury caused by Con A (ConA). CPZ (3 and 10 mg/kg) treatment 1 h before ConA injection prevented liver injury. CPZ (3, 10 mg/ig) administered 1 h after a ConA injection was also hepatoprotective, whereas cyclosporin (CsA, 100 mg/kg) was active only when given before ConA. Under either condition, CsA but not CPZ prevented concurrent increases in splenic ornithine decarboxylase (ODC) activity, a putative index of T-cell proliferation/differentiation. CPZ down-regulated tumor necrosis factor-alpha (TNF-α) and up-regulated IL-10 in mice that then received ConA, whereas delayed administration of CPZ had no effect. These results suggest that CPZ prevented liver injury without affecting the proliferation/differentiation of T-cells. The dissociation of hepatoprotection by CPZ from cytokine modulation indicates that this drug intervenes in the adherence of T-cells or the death of hepatocytes in the ConA-model.
CC 1-12 (Pharmacology)
IT **Cytoprotective agents**
(hepatoprotectants; effect of chlorpromazine and cyclosporin A on T-cell-dependent liver injury caused by Con A)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L92 ANSWER 36 OF 47 MEDLINE on STN
ACCESSION NUMBER: 97144708 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8990471
TITLE: A case of spontaneous cervical internal carotid artery dissection.

AUTHOR: **Shimada J**; Bandai H; Suzukawa K; Amou M
CORPORATE SOURCE: Department of Neurosurgery, Misato Junshin Hospital.
SOURCE: No shinkei geka. Neurological surgery, (1997 Jan) 25 (1) 67-71.
Journal code: 0377015. ISSN: 0301-2603.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970313
Last Updated on STN: 19970313
Entered Medline: 19970228

AB Dissection of the extracranial carotid artery is a recognized cause of **ischemia**, particularly in young persons who present with acute neurologic deficits, both transient and permanent. We describe a patient with a spontaneous dissection of the cervical internal carotid artery (ICA). A previously healthy 24-year-old man was hospitalized because of a sudden onset of right hemiparesis and consciousness disturbance. In reality, right cervical pain preceded this attack. The first brain MRI revealed a cerebral infarction in the right cerebral hemisphere including basal ganglia. A conventional angiography was performed 1 week later. The following angiographic picture was considered to be consistent with the diagnosis of cervical artery dissection: gradually tapered occlusion beginning distal to the carotid bifurcation. And MRA revealed the same finding. A cervical MRI revealed as an eccentric signal void (corresponding to the residual lumen) surrounded by a semilunar hyperintensity (corresponding to the mural hematoma) on T1- and T2-weighted images. Dynamic CT scan (D-CT) revealed an eccentric and crescent contrast enhancement (corresponding to the residual lumen) surrounded by a relative hypodensity compared with muscle (corresponding to the mural hematoma), itself surrounded by a thin annular enhancement. From these results, we diagnosed this patient with ICA occlusion for dissection of the extracranial carotid artery. But we decided this case contraindication of anastomosis because he had had a major stroke. Our findings suggest that MRA, cervical MRI and DCT provide early recognition of internal carotid artery dissection and monitoring of its resolution. Thus, these studies may guide clinical decisions according to the development of the dissection.

CT Check Tags: Male
Adult
Aneurysm, Dissecting: CO, complications
*Aneurysm, Dissecting: RA, radiography
*Carotid Artery, Internal: RA, radiography
Cerebral Infarction: ET, etiology
Cerebral Infarction: RA, radiography
English Abstract
Humans
Magnetic Resonance Angiography
Magnetic Resonance Imaging
Tomography, X-Ray Computed

L92 ANSWER 37 OF 47 MEDLINE on STN
ACCESSION NUMBER: 96243192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8675190
TITLE: Involvement of platelet-activating factor in cytokine production and neutrophil activation after hepatic **ischemia**-reperfusion.

AUTHOR: Serizawa A; Nakamura S; **Suzuki**; Baba S; Nakano M
CORPORATE SOURCE: Second Department of Surgery, Hamamatsu University School of Medicine, Japan.
SOURCE: Hepatology (Baltimore, Md.), (1996 Jun) 23 (6) 1656-63.
Journal code: 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960822
Last Updated on STN: 19980206
Entered Medline: 19960813

AB Although platelet-activating factor (PAF) is implicated as an important mediator in the pathogenesis of hepatic **ischemia**-reperfusion (IR) injury, the precise mechanism of its action has not been studied. We examined the hypothesis that PAF may influence neutrophils by promoting the production of tumor necrosis factor alpha (TNF-alpha) and cytokine-induced neutrophil chemoattractant (CINC), a member of the interleukin-8 (IL-8) family, and may be associated with liver and lung injury during the early phase of reperfusion after total hepatic **ischemia**. Rats pretreated with a specific PAF receptor antagonist exhibited suppression of the increase in plasma TNF-alpha and CINC levels, as well as the priming of peripheral neutrophils for superoxide production after reperfusion when compared with animals pretreated with physiological saline. These effects resulted in a reduction of plasma liver enzymes and of hepatic and pulmonary neutrophil sequestration, as well as an increased survival rate. There was a strong correlation between the time course of CINC release and hepatic or pulmonary neutrophil sequestration. We concluded that PAF activates neutrophils, either directly or by promoting the production of TNF-alpha and CINC, and is involved in hepatic IR injury.

CT Check Tags: Male
Animals
Aspartate Aminotransferases: BL, blood
*Chemokines, CXC
Chemotactic Factors: BI, biosynthesis
Chemotactic Factors: BL, blood
*Cytokines: BI, biosynthesis
Growth Substances: BI, biosynthesis
Growth Substances: BL, blood
*Intercellular Signaling Peptides and Proteins
*Liver: IN, injuries
Liver: PA, pathology
*Liver: PP, physiopathology
Lung: PA, pathology
Neutrophils: PA, pathology
*Neutrophils: PH, physiology
*Platelet Activating Factor: PH, physiology
Rats
Rats, Wistar
Reperfusion Injury: ET, etiology
Reperfusion Injury: PA, pathology
*Reperfusion Injury: PP, physiopathology
Superoxides: ME, metabolism
Tumor Necrosis Factor-alpha: BI, biosynthesis
RN 11062-77-4 (Superoxides)
CN 0 (Chemokines, CXC); 0 (Chemotactic Factors); 0 (Cytokines); 0 (Growth Substances); 0 (Intercellular Signaling Peptides and Proteins); 0

(Platelet Activating Factor); 0 (Tumor Necrosis Factor-alpha); 0 (cytokine-induced neutrophil chemoattractant, rat); EC 2.6.1.1 (Aspartate Aminotransferases)

L92 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:304946 CAPLUS
DOCUMENT NUMBER: 125:1171
TITLE: Deprenyl and pergolide rescue spinal motor neurons from axotomy-induced neuronal death in the neonatal rat
AUTHOR(S): Iwasaki, Yasuo; **Ikeda, Ken**; Shiojima, Toshiya; Kobayashi, Tomoko; Tagaya, Nozomu; Kinoshita, Masao
CORPORATE SOURCE: Ohashi Hospital, Toho University, Tokyo, 153, Japan
SOURCE: Neurological Research (1996), 18(2), 168-170
CODEN: NRESDZ; ISSN: 0161-6412
PUBLISHER: Forefront Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has been reported that both the monoamine oxidase inhibitor, deprenyl and the dopamine receptor agonist, pergolide have neuroprotective actions. To investigate the effect of deprenyl and pergolide on axotomized motor neuron death, we examined the survival of spinal motor neurons after sciatic nerve transection in the neonatal rats. Newborn rats were anesthetized with hypothermia. Sciatic nerve was cut near the obturator tendon in the left thigh. Animals were then treated daily with deprenyl (10 mg kg-1), pergolide (5 mg kg-1), or PBS for 14 days with i.p. injections in a blind fashion. After the treatment, the number of spinal motor neurons in the L4-6 was counted. There was approx. a 50% loss of spinal motor neurons in PBS-treated group. By contrast, both deprenyl and pergolide prevents spinal motor neuron death after axotomy. Co-administration of deprenyl and pergolide is more effective than either agent alone but not significant. These findings are consistent with the idea that deprenyl and pergolide are survival factors for developing spinal motor neurons.
CC 1-11 (Pharmacology)
IT **Cytoprotective agents**
(**neuroprotectants**, deprenyl and pergolide rescue spinal motor neurons from axotomy-induced neuronal death in neonatal rat)

L92 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:752508 CAPLUS
DOCUMENT NUMBER: 126:45882
TITLE: The amino-terminally truncated forms of amyloid β-protein in brain macrophages in the ischemic lesions of Alzheimer's disease patients
AUTHOR(S): Akiyama, Haruhiko; Kondo, Hiromi; Mori, Hiroshi; Kametani, Fuyuki; Nishimura, Toru; **Ikeda, Kenji**; Kato, Masanori; McGeer, Patrick L.
CORPORATE SOURCE: Tokyo Institute of Psychiatry, Tokyo, 156, Japan
SOURCE: Neuroscience Letters (1996), 219(2), 115-118
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have investigated the cerebral cortex of Alzheimer's disease in which small infarcts are found on postmortem neuropathol. examination In areas that have been subjected to recent ischemia, immunohistochem. staining for amyloid β-protein (Aβ) is much less intense than in the non-ischemic surround. However, the infiltrating brain macrophages

contain granules immunopos. for C-terminal fragments of Aβ. The immunohistochem. profile indicates that Aβ in these granules lacks epitopes in the N-terminal fragments. These data suggest that appropriately stimulated macrophages can phagocytose Aβ deposits and that digestion of the N-terminal region is an early consequence of this phagocytosis.

CC 14-10 (Mammalian Pathological Biochemistry)

IT **Brain, disease**
(**ischemia**; amino-terminally truncated forms of amyloid β-protein in brain macrophages in the ischemic lesions of Alzheimer's disease humans)

L92 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:45113 CAPLUS
DOCUMENT NUMBER: 124:164955
TITLE: CNQX prevents spinal motor neuron death following sciatic nerve transection in newborn rats
AUTHOR(S): Iwasaki, Yasuo; **Ikeda, Ken**; Shiojima, Toshiya; Kinoshita, Masao
CORPORATE SOURCE: Fourth Dep. of Internal Medicine, Toho Univ. Ohashi Hospital, Tokyo, 153, Japan
SOURCE: Journal of the Neurological Sciences (1995), 134(1,2), 21-5
CODEN: JNSCAG; ISSN: 0022-510X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid and reproducible spinal motor neuron death occurs after sciatic nerve transection in neonatal rats. This neuronal death could be due to lack of retrogradely transported target derived neurotrophic factors, such as ciliary neurotrophic factor, brain-derived neurotrophic factor, leukemia inhibitory factor and glial cell line-derived neurotrophic factor. Another hypothesis suggests that glutamate and its receptors has been implicated as possible mechanism for motor neuron death. To investigate the effect of N-methyl-D-aspartate (NMDA) and non-NMDA receptor antagonists on axotomy-induced cell death in the spinal motor neurons of neonatal rats, the authors have studied neuroprotective effects of these receptor antagonists. Newborn rats were anesthetized with hypothermia. Sciatic nerve was transected near the obturator tendon in the left thigh. Animals were then treated daily with MK-801, APV, and CNQX for 14 days with i.p. injections. Control animals received PBS in the same fashion. After the treatment, the number of spinal motor neurons in the L4-6 was counted. MK-801 and APV did not show any significant neuroprotective effect. By contrast, the number of surviving motor neurons was greater in animals that were treated with 1.0, 2.0 and 4.0 mg/kg of CNQX. This neuroprotective effect was not dose-related. The authors demonstrate the neuroprotective effect of CNQX on axotomized motor neurons, raises a possibility that such a agent may have therapeutic potential in motor neuropathy and amyotrophic lateral sclerosis.

CC 1-11 (Pharmacology)

IT **Cytoprotective agents**
(**neuroprotectants**, CNQX prevents spinal motor neuron death following sciatic nerve transection in newborn rats)

L92 ANSWER 41 OF 47 MEDLINE on STN
ACCESSION NUMBER: 95057989 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7968364
TITLE: Target-deprived CNS neurons express the NGF gene while reactive glia around their axonal terminals contain low and

high affinity NGF receptors.

AUTHOR: Junier M P; **Suzuki F**; Onteniente B; Peschanski M
CORPORATE SOURCE: INSERM CJF 91-02, Faculte Medecine, Creteil, France.
SOURCE: Brain research. Molecular brain research, (1994 Jul) 24 (1-4) 247-60.
Journal code: 8908640. ISSN: 0169-328X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 20000303
Entered Medline: 19941207

AB Reactive gliosis is part of the response of central nervous system to injury and **neurodegeneration**. Cellular components of the reactive gliosis have the capability to synthesize neurotrophic factors, and thus are capable of affecting the fate of neuronal populations in the injured tissue. In this study, we explored the putative involvement of reactive glia-derived neurotrophins in sustaining the axonal projections of target-deprived neurons. Neuronal targets of the dorsal column nuclei neurons were suppressed through excitotoxic lesion of the ventrobasal complex of the rat thalamus (VB). Despite the development of reactive gliosis, neither up-regulation of NGF, nor BDNF or NT3 mRNA could be detected by solution hybridization in the lesioned site at all times tested. In contrast, expression of the LNGFR gene increased progressively up to 90 days post-lesion. Immunocytochemical studies localized the LNGFR protein in a subset of small cells with ramified processes resembling microglia at 7 and 20 days post-lesion. At longer times, double immunolabelling studies revealed that a substantial part of LNGFR-immunoreactive cells filling the area of neuronal loss were neither microglial cells nor astrocytes although presence of LNGFR in a subset of microglial cells could not be excluded. Previous ultrastructural studies of the kainate-lesioned VB suggest that these LNGFR-immunoreactive cells correspond to oligodendrocytes and/or Schwann cells. At 2 months post-lesion, when LNGFR expression was maximal, increased levels of trkA mRNA were detected in the lesioned site. Immunocytochemical studies revealed the presence of numerous trkA-immunoreactive astrocytes. TrkB mRNA, encoding the full-length high-affinity receptor for BDNF, remained undetectable by non-isotopic in situ hybridization. In contrast to the lack of neurotrophin gene expression by glial components of the lesioned VB, dorsal column nuclei neurons contained NGF mRNA as revealed by in situ hybridization studies at 10 days--prior to enhanced LNGFR expression in the lesion--and 2 months post-lesion. In addition, the number and the staining intensity of NGF mRNA-positive neurons was increased in the target-deprived neurons, as compared with the contra-lateral nucleus projecting to intact targets. These results show that glial cells present in a reactive gliosis which develops in the kainic acid-lesioned thalamus, do not synthesize neurotrophins but instead produce high levels of both low- and high-affinity NGF receptors, LNGFR by Schwann cells/oligodendrocytes and possibly a subset of microglial cells, and trkA by reactive astrocytes.(ABSTRACT TRUNCATED AT 400 WORDS)

CT Check Tags: Comparative Study; Female
Animals
*Axons: ME, metabolism
*Brain: ME, metabolism
Brain-Derived Neurotrophic Factor
*Gene Expression
Immunohistochemistry

In Situ Hybridization
Kainic Acid: TO, toxicity
*Nerve Growth Factors: BI, biosynthesis
Nerve Tissue Proteins: BI, biosynthesis
*Neuroglia: ME, metabolism
*Neurons: ME, metabolism
Neurotrophin 3
Proto-Oncogene Proteins: BI, biosynthesis
RNA Probes
RNA, Messenger: AN, analysis
RNA, Messenger: ME, metabolism
Rats
Rats, Sprague-Dawley
Receptor Protein-Tyrosine Kinases: BI, biosynthesis
Receptor, Ciliary Neurotrophic Factor
Receptor, trkA
Receptors, Nerve Growth Factor: AN, analysis
*Receptors, Nerve Growth Factor: BI, biosynthesis
Research Support, Non-U.S. Gov't
Schwann Cells: ME, metabolism
Thalamus: DE, drug effects
Thalamus: ME, metabolism

RN 487-79-6 (Kainic Acid)
CN 0 (Brain-Derived Neurotrophic Factor); 0 (Nerve Growth Factors); 0 (Nerve Tissue Proteins); 0 (Neurotrophin 3); 0 (Proto-Oncogene Proteins); 0 (RNA Probes); 0 (RNA, Messenger); 0 (Receptor, Ciliary Neurotrophic Factor); 0 (Receptors, Nerve Growth Factor); EC 2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (Receptor, trkA)

L92 ANSWER 42 OF 47 MEDLINE on STN
ACCESSION NUMBER: 93380057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8370110
TITLE: 1,4:3,6-Dianhydrohexitol nitrate derivatives. II. Synthesis and antianginal activity of aryl- or arylcarbonylpiperazine derivatives.
AUTHOR: Hayashi H; Ikeda J; Kubo K; Moriyama T; Karasawa A; **Suzuki F**
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, Japan.
SOURCE: Chemical & pharmaceutical bulletin, (1993 Jun) 41 (6) 1100-10.
Journal code: 0377775. ISSN: 0009-2363.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931029
Last Updated on STN: 19990129
Entered Medline: 19931013

AB A series of 5-(4-aryl- or 4-arylcarbonylpiperazin-1-yl)-5-deoxy-1,4:3,6-dianhydro-L-iditol 2-nitrates was prepared in order to obtain orally active, nitrate-type vasodilators with reduced side effects. Our drug design was based on a small reduction in the lipophilicity compared to that of 5-deoxy-5-[4-(3-phenylthiopropyl)piperazin-1-yl]-1,4:3,6-dianhydro-L-iditol 2-nitrate (1, KF14124). Compounds 4h (aryl = benzimidazol-2-yl), 4i (arylcarbonyl = nicotinoyl), and 4w (arylcarbonyl = 3-furoyl) showed potent anti-**ischemic** activity in a lysine-vasopressin-induced angina pectoris model (rats), and their

structure-activity relationships are discussed. Compound 4i exhibited potent vasodilation of the coronary artery in anesthetized dogs and also exhibited potent preload reduction in a heart failure model (dogs) as compared with isosorbide dinitrate (2), nicorandil (3), and KF14124 (1). Furthermore, 4i showed much weaker acute lethal toxicity and less central nervous system depression than 1 in mice. Thus, 4i (KW-3196) is under development as a vasodilator and a drug for treating angina pectoris.

CT Check Tags: Comparative Study; Female; Male
*Angina Pectoris: DT, drug therapy
Animals
Central Nervous System: DE, drug effects
Disease Models, Animal
Dogs
Drug Design
Heart Failure, Congestive: DT, drug therapy
*Isosorbide Dinitrate: AA, analogs & derivatives
Isosorbide Dinitrate: CS, chemical synthesis
Isosorbide Dinitrate: CH, chemistry
*Isosorbide Dinitrate: PD, pharmacology
Isosorbide Dinitrate: TU, therapeutic use
Lypressin: DU, diagnostic use
Mice
***Myocardial Ischemia: DT, drug therapy**
Piperazines: CS, chemical synthesis
Piperazines: CH, chemistry
*Piperazines: PD, pharmacology
Piperazines: TU, therapeutic use
Rats
Rats, Wistar
Structure-Activity Relationship
Vasodilator Agents: CS, chemical synthesis
Vasodilator Agents: CH, chemistry
*Vasodilator Agents: PD, pharmacology
Vasodilator Agents: TU, therapeutic use

RN 134186-26-8 (KF 14124); 50-57-7 (Lypressin); 87-33-2 (Isosorbide Dinitrate)

CN 0 (Piperazines); 0 (Vasodilator Agents)

L92 ANSWER 43 OF 47 MEDLINE on STN
ACCESSION NUMBER: 93380056 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8370109
TITLE: 1,4:3,6-Dianhydrohexitol nitrate derivatives. I. Synthesis and antianginal activity of alkylpiperazine derivatives.
AUTHOR: Hayashi H; Ikeda J; Kuroda T; Kubo K; Sano T; **Suzuki F**
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, Japan.
SOURCE: Chemical & pharmaceutical bulletin, (1993 Jun) 41 (6) 1091-9.
Journal code: 0377775. ISSN: 0009-2363.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931029
Last Updated on STN: 19960129
Entered Medline: 19931013

AB A series of 5-deoxy-5-(4-substituted piperazin-1-yl)-1,4:

3,6-dianhydro-L-iditol 2-nitrates was prepared and evaluated for oral anti-**ischemic** activities. Inhibition of lysine-vasopressin-induced T-wave elevation in the electrocardiogram (ECG) of rats (angina pectoris model) served as a primary assay. Optimum activity was observed for the compounds with the aryl-heteroatom (O,S, or N)-propyl group. Among them, the phenylthiopropyl-substituted compound 13 exhibited the most potent activity. Furthermore, intraduodenal administration (i.d.) of 13 tended to decrease left ventricular end-diastolic pressure (LVEDP) in a propranolol-induced heart failure model (dogs) and showed a potent protective effect against reperfusion arrhythmia in rats. Thus, 13 (KF 14124) is under further study as an orally active nitrate.

CT Check Tags: Female; Male
Administration, Oral
*Angina Pectoris: DT, drug therapy
Animals
Anti-Arrhythmia Agents: CS, chemical synthesis
*Anti-Arrhythmia Agents: PD, pharmacology
Anti-Arrhythmia Agents: TU, therapeutic use
Blood Pressure: DE, drug effects
Disease Models, Animal
Dogs
Electrocardiography: DE, drug effects
Heart Failure, Congestive: DT, drug therapy
Heart Rate: DE, drug effects
*Isosorbide Dinitrate: AA, analogs & derivatives
Isosorbide Dinitrate: CS, chemical synthesis
*Isosorbide Dinitrate: PD, pharmacology
Isosorbide Dinitrate: TU, therapeutic use
Lypressin: PD, pharmacology
Piperazines: CS, chemical synthesis
*Piperazines: PD, pharmacology
Piperazines: TU, therapeutic use
Propranolol: TO, toxicity
Rats
Rats, Wistar
Vasodilator Agents

RN 134186-26-8 (KF 14124); 50-57-7 (Lypressin); 525-66-6 (Propranolol); 87-33-2 (Isosorbide Dinitrate)

CN 0 (Anti-Arrhythmia Agents); 0 (Piperazines); 0 (Vasodilator Agents)

L92 ANSWER 44 OF 47 MEDLINE on STN

ACCESSION NUMBER: 92217103 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1806275

TITLE: Synthesis and biological activity of 11-[4-(cinnamyl)-1-piperazinyl]- 6,11-dihydrodibenz[b,e]oxepin derivatives, potential agents for the treatment of cerebrovascular disorders.

AUTHOR: **Kurokawa M**; Sato F; Masuda Y; Yoshida T; Ochi Y; Zushi K; Fujiwara I; Naruto S; Uno H; Matsumoto J

CORPORATE SOURCE: Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Osaka, Japan.

SOURCE: Chemical & pharmaceutical bulletin, (1991 Oct) 39 (10) 2564-73.
Journal code: 0377775. ISSN: 0009-2363.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199205

ENTRY DATE: Entered STN: 19920529
Last Updated on STN: 20000303
Entered Medline: 19920514

AB A series of 11-[4-(cinnamyl)-1-piperazinyl]-6,11-dihydrodibenz[b,e] oxepins and related compounds were synthesized and evaluated for their protective activities against complete **ischemia**, normobaric hypoxia, lipidperoxidation and convulsion. Structure-activity relationship studies of this series led to the finding of (E)-1-(3-fluoro-6,11-dihydrodibenz[b,e]oxepin-11-yl)-4-(3-phenyl-2-propenyl)piperazine dimaleate (50), AJ-3941 with the most appropriate property for combined pharmacological activities. Compound 50 also shows an inhibitory effect against cerebral edema as well when orally given to rats.

CT Animals
*Benzothiepins: CS, chemical synthesis
Benzothiepins: PD, pharmacology
Benzothiepins: TU, therapeutic use
*Benzoxepins: CS, chemical synthesis
Benzoxepins: PD, pharmacology
Benzoxepins: TU, therapeutic use
Brain Edema: DT, drug therapy
Brain Ischemia: DT, drug therapy
*Cerebrovascular Disorders: DT, drug therapy
Flunarizine: PD, pharmacology
Flunarizine: TU, therapeutic use
Hypoxia, Brain: DT, drug therapy
Mice
*Piperazines: CS, chemical synthesis
Piperazines: PD, pharmacology
Piperazines: TU, therapeutic use
Rats
Structure-Activity Relationship

RN 52468-60-7 (Flunarizine)
CN 0 (Benzothiepins); 0 (Benzoxepins); 0 (Piperazines)

L92 ANSWER 45 OF 47 MEDLINE on STN
ACCESSION NUMBER: 89104624 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3214233
TITLE: A case of spinal arachnoid cyst associated with vascular anomaly and repeated transient paraparesis after surgery.
AUTHOR: Takeichi Y; Saito A; **Suzuki F**; Koyama T
SOURCE: Nippon geka hokan. Archiv fur japanische Chirurgie, (1988 Jul 1) 57 (4) 309-15.
Journal code: 0421143. ISSN: 0003-9152.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890222

CT Check Tags: Male
*Arachnoid
Arteries: AB, abnormalities
Cysts: CO, complications
*Cysts: SU, surgery
English Abstract

Humans
***Ischemia: ET, etiology**
Middle Aged
*Paralysis: ET, etiology
*Postoperative Complications
*Spinal Cord: BS, blood supply
Spinal Cord Diseases: CO, complications
*Spinal Cord Diseases: SU, surgery

L92 ANSWER 46 OF 47 MEDLINE on STN
ACCESSION NUMBER: 88223733 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3286043
TITLE: Intracardiac generation of angiotensin and its physiologic role.
AUTHOR: Lindpaintner K; Jin M; Wilhelm M J; **Suzuki F**; Linz W; Schoelkens B A; Ganten D
CORPORATE SOURCE: German Institute for High Blood Pressure Research, University of Heidelberg, F.R.G.
SOURCE: Circulation, (1988 Jun) 77 (6 Pt 2) I18-23. Ref: 56
Journal code: 0147763. ISSN: 0009-7322.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880629

AB The emerging recognition of the existence and potential biological significance of local tissue renin-angiotensin systems in a number of organs has fostered interest in a possible intrinsic cardiac renin-angiotensin system. Evidence for such a system was first provided by biochemical measurements of components of the renin-angiotensin system in cardiac tissue. It has recently been demonstrated that the genes coding for renin and angiotensinogen are expressed in all regions of the heart, an essential prerequisite for the postulated intracardiac biosynthesis of these proteins. Moreover, we have shown the presence of a functional and physiologically active pathway for the conversion of angiotensin I to angiotensin II in the beating mammalian heart. This conversion appears to be catalyzed by a specific cardiac converting enzyme that is susceptible to systemically administered converting-enzyme inhibitors. Evidence for the physiologic importance of the cardiac renin-angiotensin system comes from experimental data as well as indirect clinical evidence. The potent coronary vasoconstrictor properties of angiotensin II underscore its possible significance in myocardial **ischemia** and **ischemic** heart disease, in particular when viewed in the context of selective local activation. The long-known positive inotropic effects of angiotensin II are based on its direct myotropic properties and on its facilitatory effects on sympathetic neurotransmission and may be of added significance in metabolically compromised states. We have recently demonstrated that locally generated angiotensin may be a dominant etiologic factor in the pathogenesis of reperfusion arrhythmias. In addition, we have found experimental evidence for a deleterious effect of angiotensin II on myocardial metabolism in the setting of regional myocardial **ischemia**.(ABSTRACT TRUNCATED AT 250 WORDS)

CT *Angiotensin II: BI, biosynthesis

Angiotensin II: PH, physiology
Animals
*Heart: PH, physiology
Renin: PH, physiology
Renin-Angiotensin System
Research Support, Non-U.S. Gov't
RN 11128-99-7 (Angiotensin II)
CN EC 3.4.23.15 (Renin)

L92 ANSWER 47 OF 47 MEDLINE on STN
ACCESSION NUMBER: 69268459 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5817122
TITLE: Spatial velocity electrocardiography in **ischemic** heart diseases. Repolarization and direction of the maximum T vector.
AUTHOR: Sano T; Hiroki T; Hazama H; **Suzuki F**
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (1969 Mar) 27 (3) 677-80.
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196910
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19900101
Entered Medline: 19691007
CT *Coronary Disease: PP, physiopathology
*Electrocardiography
Humans
*Vectorcardiography